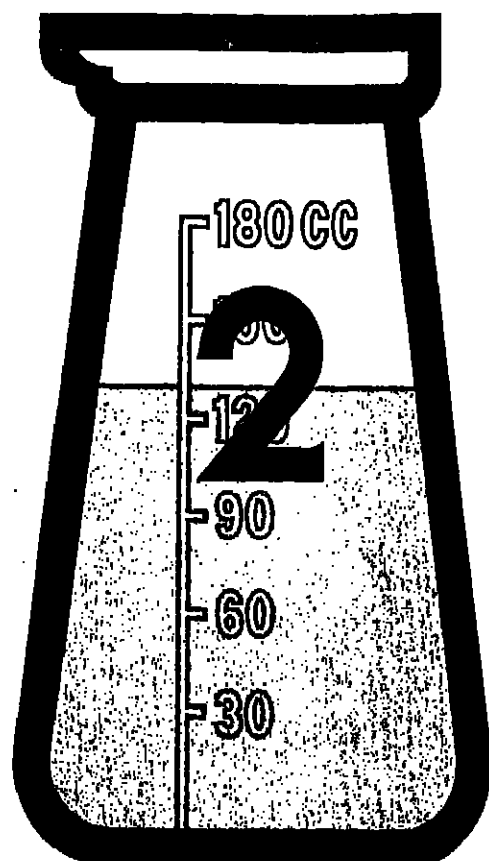


Adequate
fluid
intake



Frequent
voiding

The 3rd Basic

Gantanol (sulfamethoxazole) B.I.D.

4 tablets (0.5 Gm each) STAT—then
2 tablets B.I.D. for 10-14 days

Basic therapy with
convenience for acute
nonobstructed cystitis

- Effective against susceptible *E. coli*, *Klebsiella-Aerobacter*, *Staph. aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms.

Note: Carefully coordinate in vitro sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions; agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical

signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, lactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, asthmalike and allergic myocarditis); gastrointestinal reactions (nausea, anorexia, abdominal pain, hepatitis, diarrhea, proctitis, pancreatitis and stomatitis); CNS reactions (headache, dizziness, neuritis, mental depression, convulsions, ataxia, halluci-

nations, tinnitus, vertigo and insomnia); miscellaneous reactions (drug fever, chills, toxic nephrosis with oliguria and anuria, periarthritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogenic diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm b.i.d. or t.i.d., depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs b.i.d. Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Medical Tribune

(1976, Medical Tribune, Inc.)

and Medical News

Vol. 17, No. 21

world news of medicine and its practice—fast, accurate, complete

Wednesday, June 9, 1976

Better Screening Urged

Gestational Diabetes Held Underdiagnosed

By FRANCES GOODNIGHT
Medical Tribune Staff

New York—Better screening of pregnant women to detect gestational diabetes was urged here by a Case Western Reserve investigator who said this condition "frequently" remains unsuspected even though it occurs in 1% to 25% of all pregnancies.

Dr. Irwin R. Merkatz, Professor of Obstetrics and Gynecology, pointed out that such an incidence far exceeds that of overt diabetes. And expressing concern over risk to the fetus, he cited one estimate that as many as 4,500 pregnancies per year result in perinatal death from undiagnosed or untreated gestational diabetes.

"Therefore, the importance of screening for abnormal glucose tolerance during pregnancy must be re-emphasized," he said at a symposium on

Continued on page 3

New Study Poses Question

Chubby Infants: Is Early Dieting Worthwhile?

By MICHAEL HERRING
Medical Tribune Staff

St. Louis—A new study comparing infant and adult weight status in a selected population shows that although chubby six-month-olds are more likely to become overweight or obese adults than normal or light weight infants, only a minority (36%) will actually become so, according to a Johns Hopkins investigator.

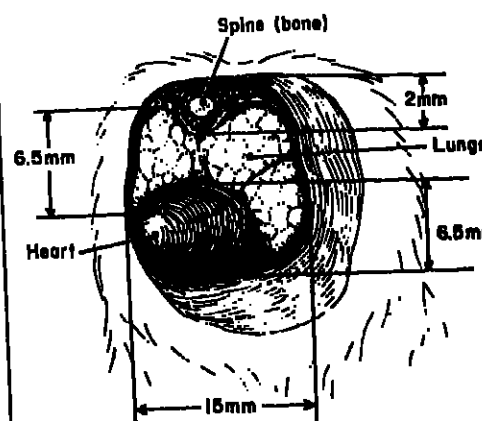
Moreover, Dr. Evan Charney told the Ambulatory Pediatric Association, the weight attained in the first six months, while it is more predictive of adult obesity than weight at birth or rate of gain, may not be causal at all, but only "the expression of some genetic predisposition."

These findings raise the question of whether overweight infants should be put on diets at such a crucial time in their development, in hopes of warding off later obesity. The resulting stress on both parents and child could be "psychologically hazardous" or could "impair brain or other organ system development," Dr. Charney cautioned.

A study conducted at the University of

Continued on page 23

Scanning Radio Signals from Living Tissue



Using radio signal emissions of living tissue, a New York team has visualized internal structures and tumors in animals. Photo shows radio-frequency scan of hydrogen atoms in mouse thoracic cavity. Heart appears as brightest area, since it has highest water ratio. Dr. R.V. Damadian, Downstate Medical Center, says noninvasive system can be "tuned" for almost any element, ultimately enabling clinicians to visualize a tumor and obtain chemical data about it in early diagnostic studies.

Bell's Palsy: A Virus-Caused Form of Cranial Polyneuritis?

By ANASTASIA TOUPRIS
Medical Tribune Staff

New York—A controversial new theory of Bell's palsy as a variant of cranial polyneuritis caused by a virus was recently expounded here by a specialist in facial paralysis. This new concept of the disease and the relatively new steroid treatment regimen, which when begun early enough leads to recovery in 94% of patients, are leading physicians to rethink traditional views of the illness.

"Bell's palsy is not a localized dis-

ease of the seventh cranial nerve but represents a variant of acute benign cranial polyneuritis, possibly caused by the herpes simplex virus," says Dr. Kedar K. Adour, chairman of the Facial Paralysis Research Clinic at the Kaiser-Permanente Medical Center in Oakland, Calif.

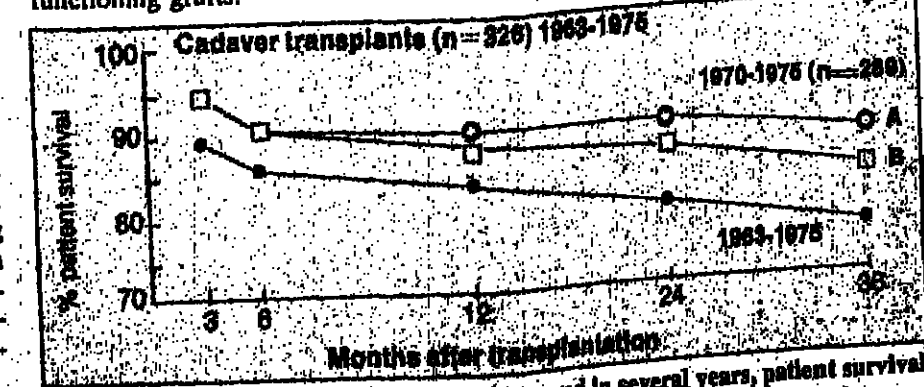
In an interview with MEDICAL TRIBUNE following a lecture at the Neurological Institute at Columbia-Presbyterian Medical Center in New York, Dr. Adour, an otolaryngologist, dis-

Continued on page 15

Cadaver Kidney Graft Survival 23% But Patient Survival Is Enhanced

By HARRIET PAGE
Special Tribune Correspondent

SAN FRANCISCO—By the end of five years, 644 of every 1,000 patients who receive cadaver kidney transplants will have been returned to dialysis, 126 will have died, and only 230 will have functioning grafts.



Although graft survival (23%) has not improved in several years, patient survival at Rogosin Kidney Center in New York has been enhanced, as shown above.

27,000 in Field Trials

Pneumococcal Vaccine Found Safe, Effective

By NATHAN HORWITZ
Medical Tribune Staff

ATLANTIC CITY, N.J.—International field trials of a polyvalent pneumococcal pneumonia vaccine have given an "unequivocal demonstration" of the vaccine's efficacy in preventing pneumonia and bacteremic pneumococcal infection, a multi-center team reported here.

The vaccine was shown to be "safe, antigenic and at least 78.5% effective in providing protection" against type-specific pneumococcal pneumonia, and more than 82% effective against bacteremic infection, in studies of 12,000 young South African goldminers, said Dr. Robert Austrian of the University of Pennsylvania.

Further, preliminary findings in ongoing studies of approximately 15,000 subjects in North Carolina and in San Francisco, he stated, are, thus far, "consistent with the results in South Africa in showing the vaccine's efficacy."

Dr. Austrian, who is Professor and Chairman of Research Medicine, said

Continued on page 3

making
rounds
at
press
time

VOID MALPRACTICE LAW—Illinois State Supreme Court has struck down legislature's 1975 malpractice act, calling it "unconstitutional" to set \$500,000 as maximum that patient can recover in lawsuit. High bench also overturned provision allowing a doctor to sit on pretrial review panel. In finding for patient who charged she suffered permanent injury in gynecologic operation, Court contended that singling out only medical malpractice actions for maximum awards constitutes "a special privilege" in violation of state constitution. Medical society spokesman says that group will abandon effort to put legal lid on awards.

WHEN THE SYMPTOMS ARE CLEAR BUT THE CAUSE IS NOT...

A FREQUENTLY EFFECTIVE AGENT FOR "GRAY AREA" SYMPTOMS IN THE ELDERLY PATIENT

• CONFUSION • LACK OF SELF-CARE • DIZZINESS
• MOOD-DEPRESSION • UNSOCIABILITY

Many elderly patients suffering "gray area" symptoms not attributable to any specific disease can be helped with Hydergine therapy. And, relief of such symptoms, no matter how modest, often allows patients to function better on their own and to re-establish positive relations with the people around them.

Contraindications: Hypersensitivity to the drug.
Precautions: Because the target symptoms are of unknown etiology, careful diagnosis should be attempted before prescribing Hydergine sublingual tablets.
Adverse Reactions: Serious side effects have not been found. Some sublingual irritation, transient nausea, and gastric disturbances have been reported. Hydergine sublingual tablets do not possess the vasoconstrictor properties of natural ergot alkaloids.
Dosage and Administration: 1 mg sublingually three times daily. Alleviation of symptoms is usually gradual and results may not be observed for 3-4 weeks.

HYDERGINE®

SUBLINGUAL TABLETS

Each 1-mg Hydergine sublingual tablet contains dihydroergocornine 0.333 mg, dihydroergocristine 0.333 mg, and dihydroergocryptine 0.333 mg, as the mesylates, representing a total of 1.0 mg.

A SINGLE 1-mg SUBLINGUAL TABLET THREE TIMES A DAY MEETS THE PROPER 3-mg TOTAL DAILY HYDERGINE DOSE

SANDOZ PHARMACEUTICALS, INC., KANAWHA, N.J. 07096

Wednesday, June 9, 1976

Pneumococcal Vaccine Shown 'Safe', At Least 78% Effective

Continued from page 1
The data raise the realistic prospect that a polyvalent pneumococcal pneumonia vaccine would "largely eliminate" pneumococcal pneumonia among American adults. He spoke at the annual meeting of the American Association of Physicians.

In the South African trials, started in 1970, goldmining novices were chosen because pneumonia is still endemic in this population. "The attack rate of putative pneumococcal pneumonia among men coming to work for the first time in the mine was found [in a preliminary study] to be 90 per 1,000 man-years of exposure," Dr. Austrian said.

The 12,000 young adult males were randomized to receive either a polyvalent pneumococcal vaccine, a Group A meningococcal vaccine or a saline placebo. Three polyvalent pneumococcal vaccines were studied, one with capsular polysaccharides of six pneumococcal types, the other two with 13 pneumococcal types.

The combined data for the three trials demonstrated that the vaccines were effective, in the ratios stated earlier, in preventing bacteremic pneumococcal infection caused by the types included in the preparation, and type-specific putative pneumococcal pneumonia.

No Replacement Illness

A major finding, Dr. Austrian told the meeting, was the demonstration, for the first time, that other pneumococcal illnesses have not taken the place of those prevented by the vaccine.

"Throughout the course of our investigation," he stated, "the question has been raised repeatedly whether or not disease eliminated by prevention of infection with selected pneumococcal types would lead to its replacement by illness caused by other pneumococcal types. . . . The attack rate of radiologically confirmed pneumonia in pneumococcal vaccinees [two years after the start of the trial] has been reduced to slightly more than half, and it has been shown that this reduction has been maintained over a period of a year in a closed population into which new potentially susceptible subjects were being introduced. Whether or not the reduction would be maintained indefinitely cannot be ascertained at this time."

Side effects in the trials were relatively minor, he said. These included some discomfort or pain at the site of injection, local erythema lasting for a day, and a slight temperature elevation for one day.

Dr. Austrian reported that a dodecavalent pneumococcal vaccine is expected to be licensed within the next year, and "should provide a useful prophylactic agent for adults at higher than average risk of a fatal outcome of pneumococcal infection."

If a 20-antigen vaccine were to be used widely, he added, "the prospect of largely eliminating the half million pneumococcal pneumonias estimated to occur annually in the adult population of this country would appear to be a realizable one."

Coauthors were Drs. Robert M.

Douglas, University of Pennsylvania, Gerald Schiffman, Downstate Medical Center, New York, Albert M. Cofrancesco, Pretoria, South Africa, Hendrik J. Koornhof and Stanley Hayden-Smith, South African Institute for Medical Research, Johannesburg, and Robert D. W. Reid, Hospital of the East End Proprietary Mine, South Africa.

Related Findings

In a related paper, a University of Illinois investigator reported that a controlled randomized trial of a polysaccharide vaccine with eight antigens significantly reduced the carrier state among a sampling of Chicago's Skid Row population.

The findings were based on studies of 297 subjects in a total group of 3,300 volunteers who are undergoing the vaccine trial. Controls received tetanus toxoid inoculations.

H. E. Krause, M.P.H., told the American Federation for Clinical Research here that acquisition of the carrier state was defined as the initial recovery from the sputum of volunteers

of the same capsular type in each of two weeks or more during a given month.

"Acquisition of capsular types contained in the vaccine occurred in 35 or 25.5% of the 137 tetanus toxoid vaccinees, but in only 24 or 15% of the 160 pneumococcal vaccinees; this difference represented a 41% reduction in acquisition of vaccine types among pneumococcal vaccinees compared to tetanus toxoid vaccinees," Ms. Krause declared.

Duration of the carrier state was also significantly longer in the control group, the investigator said. "The mean duration of carriage, irrespective of vaccine type, was 2.4 months in pneumococcal vaccinees and 4.3 months in tetanus toxoid vaccinees."

These findings show, Ms. Krause concluded, that pneumococcal polysaccharide vaccine can stimulate protective antibody and thus provide "the basis for concluding that the vaccine will be effective in reducing pneumonia rates as well."

Coauthor was Dr. M. A. Mufson.

Better Screening Urged to Detect Gestational Diabetes

Continued from page 1

diabetes and other endocrine disorders presented by Cornell University Medical Center and sponsored by the National Foundation-March of Dimes.

Clinicians should be alert to the possibility of gestational diabetes, Dr. Merkatz believes, if the pregnant woman has a family history of diabetes, or if she is obese—particularly if she is over the age of 25. Other suggestive circumstances include a previous pregnancy outcome of unexplained stillbirth, neonatal death, a baby that weighed more than 4,000 grams, or one with a major anomaly.

The presence of glucose in a second fasting urine specimen or an observation of clinical hydranionosis should also raise suspicions, he added.

But Dr. Merkatz cautioned that the diagnosis of gestational diabetes is "contingent upon the presence of an abnormal glucose tolerance test," and called such testing advisable for all pregnant women.

3rd Trimester Glucose Load

What he recommends is administration of an oral 50-gram glucose load in the third trimester, when insulin antagonism is most likely to unmask mild carbohydrate intolerance. An earlier test would be "prudent" in patients thought to be at risk but should be repeated later, he said.

Dr. Merkatz defines the criterion for diagnosis of gestational diabetes in the third trimester as two or more values equal to or greater than the following whole blood glucose concentrations: 90 mg/deciliter fasting; 165 mg/dl at one hour; 145 mg/dl at two hours; and 125 mg/dl at three hours.

Stressing the need for strict control of the maternal glucose level in both overt and gestational diabetes, Dr. Merkatz said the goal adopted at MacDonald House—a maternity and gynecologic unit of University Hospitals of

Cleveland—is to maintain fasting blood glucose concentrations under 100 mg/dl and postprandial levels approximately 120 mg/dl.

Ambulatory management is supplemented by "liberal use of hospitalization" for clinical evaluation and control. Predelivery hospitalization is employed routinely at 34-35 weeks for the insulin-dependent diabetic and for the gestational diabetic if there has been late diagnosis or evidence of poor control or developing pregnancy complications.

Fetal Surveillance

Fetal surveillance begins with ultrasonography in the mid trimester for early determination of fetal age, and includes a range of monitoring procedures such as hormonal assessment of fetal-placental function, periodic amniocenteses for evaluation of fetal pulmonary maturity, and electronic monitoring of fetal heart rate.

In 1974-1975, 96 diabetics (68 gestational, 28 insulin-dependent before pregnancy) were delivered at the hospital with a perinatal mortality rate of only 4.2%.

By comparison, 52 of the gestational diabetics had previously had a total of 133 potentially viable pregnancies with a perinatal mortality rate of 8.3%. For the 171 prior pregnancies of all 70 parous gestational and insulin-dependent diabetics, the combined rate had been 13.5%.

New Hearing Aid Rules?

Medical Tribune Report

WASHINGTON, D.C.—The Food and Drug Administration has proposed labeling requirements and conditions of sale for hearing aids that would require a medical examination before purchase if the patient has dizziness, ear deformity, fluid drainage, rapid onset of hearing loss, a foreign body in the ear, or other "warning signals."

index

CLINICAL NEWS NOTE: "...the problem facing nephrologists is to offer their patients all the possible alternatives. Since we still cannot predict success or failure on an individual basis, there is always a possibility that a [cadaver kidney] graft in a poor risk patient will succeed. The decision to go ahead with such a procedure must depend on a low mortality rate and an informed decision by the patient." (Dr. William T. Stubenbord. See page 1.)

Medicine: 1, 19, 21

Pneumococcal vaccine shown effective, safe 1
Bell's palsy seen as virus-caused cranial polyneuritis 1
Cadaver kidney graft survival projected at 23% after 5 years 1
Gestational diabetes held underdiagnosed 1
Tea may block absorption of vitamin B₁ 19
Phenol burn therapy includes use of glycol solvent 21

Pediatrics: 1

Overweight infants: 36% become overweight adults 1

feature index

Editorial Capsules 8
Letters to Tribune 11
Editorials 19
Medicine on Stamps 19
One Man and Medicine 20
Current Opinion 22
Elliot Janoway 22
Immunaria Medica 31

Introducing a new feature...

INTERNATIONAL REPORT

from Britain, France, Germany, Japan

A roundup of significant clinical news as reported by MEDICAL TRIBUNE's foreign editions.

See Page 17

Medical Tribune

ARTHUR M. SACKLER, M.D.
International Publisher

Advisory Board

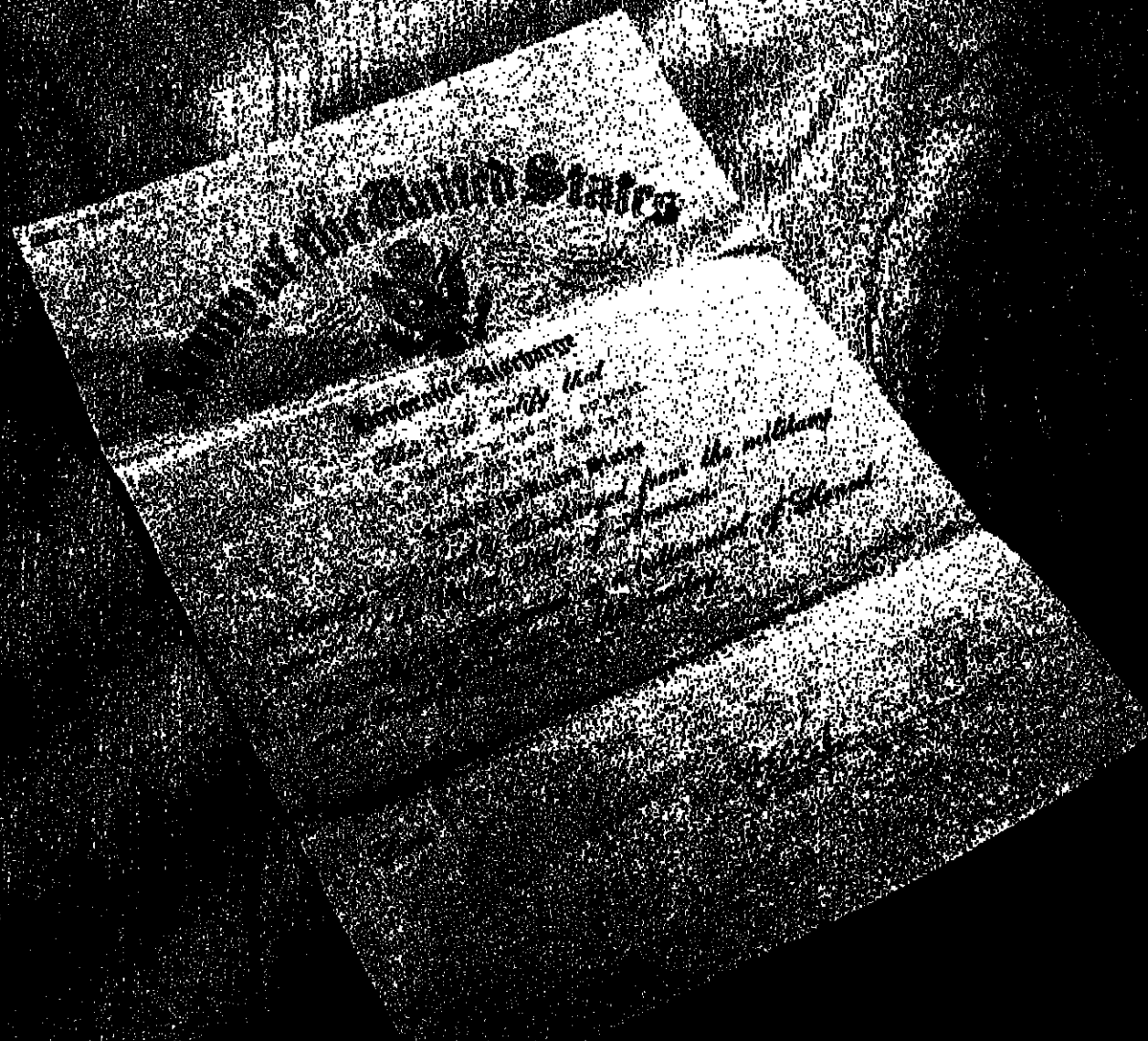
JOHN ADRIANI, M.D. • RENE J. DUBOS, Ph.D.
JULIUS H. MASSERMAN, M.D.
BERNARD LOWN, M.D.
ALTON OCHSNER, M.D. • LEO G. RIGLER, M.D.

HARRY HENDERSON, M.D. • RICHARD GUNNER, M.D.
Editor-in-Chief Associate Editor
CHRIS WOODBURY, Ph.D. HAROLD POSNOT
General Manager Executive News Editor
JOHN H. HEWITT NATHAN HORWITZ
Associate News Editor Special News Editor
WILLIAM PRITTS AMY CONNER
Art Supervisor Picture Editor

880 Third Avenue, New York, N.Y. 10022
Phone (212) 421-4000 • Audited by Business Publications Audit of Circulation, Inc.

MEDICAL TRIBUNE is published each Wednesday except on June 16, 30; July 14, 28; Aug. 11, 25; Sept. 29; Dec. 1, 22, 29, by Medical Tribune, Inc., 880 Third Avenue, New York, N.Y. 10022. Controlled circulation postage paid at Vineland, N.J. 08360. Subscription \$29.00, Students \$7.50.

After 20 years, 523 veterans "re-enlisted" for a special assignment...



The assignment: combat hypertension

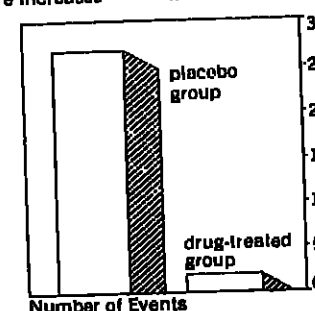
The VA studies^{1,2} showed it had to be controlled.

Long after World War II, large numbers of veterans were enrolled in what have since become known as landmark studies in the treatment of hypertension.

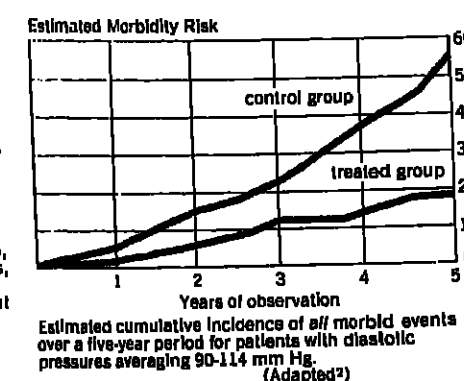
The VA studies^{1,2} established that even moderately elevated blood pressure increases the risk of target-organ damage and death—and that hypertension should be treated in order to reduce morbidity.

In the earlier study¹, covering a two-year period, 143 male veterans with diastolic pressures averaging 115 through 129 mm Hg were randomly assigned to either placebo or active treatment. The study showed significant

benefits to the drug-treated group. The second study² covered a five-year period and involved 380 patients with mild to moderate hypertension (diastolic pressures averaging 90 through 114 mm Hg). Here, too, active drug treatment was beneficial; thus the estimated five-year risk of developing a morbid event was reduced from 55% to 18%.²



In the placebo-treated group, there were 27 morbid events, 4 of them fatal; in the drug-treated group, there were but two complicating events. (Adapted¹)



Control was achieved with:

hydrochlorothiazide

which provides a mild antihypertensive effect through fluid volume control; potentiates the activity of other antihypertensive agents.³⁻⁵

(a) Symbolized reduction in circulating fluid volume

plus hydralazine

the unique action of oral hydralazine lowers blood pressure through direct arteriolar vasodilation to reduce peripheral resistance.³⁻⁵

(c) Diagram of relaxed arteriole

plus reserpine

which lowers blood pressure through sympathetic inhibition;³⁻⁵ also produces a central sedative effect which may prove particularly useful in the management of the stress-reactive patient.

(b) Schema of norepinephrine depletion at sympathetic nerve ending

Only one antihypertensive agent contains all three components used in two published VA cooperative studies.^{1,2}

In the VA studies, Ser-Ap-Es itself was not used. However, all the components of Ser-Ap-Es were used in varying combinations.^{1,2}

Ser-Ap-Es contains all the antihypertensive medication many patients will need.

And when the dosage of each component corresponds to the dosage preestablished by

individualized titration, Ser-Ap-Es may prove more convenient and more economical.

The basic drugs used in the VA studies—hydro-

chlorothiazide, reserpine, and hydralazine—are original products of CIBA research.

Note: Use Ser-Ap-Es cautiously in patients with advanced renal damage or cerebrovascular accident. Discontinue at first sign of mental depression.

Please turn page for brief prescribing information.

Ser-Ap-Es

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

C I B A

References
 1. Effects of treatment on morbidity in hypertension. Results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 202:1026-1034, 1967.
 2. Effects of treatment on morbidity in hypertension. II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 213:1543-1548, 1970.
 3. Russell RP: Hypertension. In Harvey AM, Johns RJ, Owens AH, et al (eds): *The Hypertension Practice of Medicine*, ed 18. New York, Appleton-Century-Crofts, 1972, pp 331-334.
 4. Gifford RW Jr: Drugs for arterial hypertension. In Modell W (ed): *Drugs of Choice*, 1972-1973, ed 1. St. Louis, CV Mosby Co, 1972, pp 580-593.
 5. Sellers AM, Itzkowitz HD, Lindner AG: Systemic arterial hypertension. In Conn HL Jr, Philadelphia, Lea & Febiger, 1971, vol 1, pp 934-943.

Ser-Ap-Es®

reserpine 0.1 mg
 hydralazine hydrochloride 25 mg
 hydrochlorothiazide 16 mg

WARNING:
 This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy directed to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

INDICATIONS:
 Hypertension. (See box warning.)
CONTRAINDICATIONS:
 Reserpine: Known hypersensitivity; mental depression (especially with suicidal tendencies); active peptic ulcer; ulcerative colitis; electroconvulsive therapy.
 Hydralazine: Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.
 Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.
WARNINGS:
 Reserpine: Use with extreme caution in patients with a history of mental depression. Discontinue at first sign of depression, early morning insomnia, loss of appetite, impotence, or self-deprecation. Drug-induced depression may persist for several months after withdrawal and may be severe enough to result in suicide. MAO inhibitors should be avoided or used with extreme caution.
 Hydralazine: Hydralazine may produce in a few patients a clinical picture simulating systemic lupus erythematosus. In such patients hydralazine should be discontinued unless the benefits to risk determination requires continued antihypertensive therapy with this drug. Symptoms and signs usually regress when the drug is discontinued but residues have been detected many years later. Long-term treatment with steroids may be necessary.
 Ciba's L.E. cell preparations, and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy with hydralazine or if the patient develops any unexplained signs or symptoms.
 A positive antinuclear antibody titer and/or positive L.E. cell reaction requires that the physician carefully weigh the implications of the test results against the benefits to be derived from antihypertensive therapy with hydralazine.
 Use MAO inhibitors with caution.
 Hydrochlorothiazide: Use with caution in severe renal disease. In patients with renal disease, hydralazine may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.
 Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.
 Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potential adverse effects of hydralazine especially with reference to myocardial activity.
 Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is a water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.
 Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.
 Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.
 Thiazides may decrease the responsiveness to tuberculin. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.
 If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.
 Thiazides may decrease serum PBI levels with digitalis and quinidine.
ADVERSE REACTIONS:
 Reserpine: Gastrointestinal—hypersecretion; nausea; vomiting; anorexia; diarrhea. Cardiovascular—angina-like symptoms; arrhythmias (particularly when used concurrently with digitalis or quinidine); bradycardia. Central Nervous System—depression; depression; nervousness; paraesthesia; nightmares; parkinsonian syndrome; and other extrapyramidal tract symptoms. CNS sensitization (manifested by dull sensorium, deafness, glaucoma, vertigo, and optic atrophy). Miscellaneous—frequently nasal congestion; pruritus; rash; dryness of mouth; dizziness; headache; dyspnea; syncope; epistaxis; purpura and other hemorrhagic reactions; impotence or decreased libido; weight gain; breast engorgement; pseudotumor; gynecomastia; rarely water retention with peripheral edema.
 Hydralazine: Common—headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. Less frequent—facial peripheral neuritis, evidenced by paraesthesia, numbness, and tingling; edema; dizziness; lightheadedness; depression; psychologic reactions characterized by depression, disorientation, or anxiety; fever; chills; arthralgia; eosinophilia; and, rarely, hepatitis; constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; reduction in hemoglobin and red cell count; leukopenia; agranulocytosis, and purpura.
 Hydrochlorothiazide: Gastrointestinal—angry, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestasis), pancreatitis. Central Nervous System—dizziness, vertigo, paraesthesia, headache, xanthopsia. Dermatologic—hypersensitivity—purpura, photosensitivity, rash, urticaria, necrotizing angitis. Stevens-Johnson syndrome, and other hypersensitivity reactions. Hematologic—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. Cardiovascular—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Other—hyperuricemia, glycosuria, hypercalcemia, muscle spasms, weakness, redness, when severe adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

DOSEAGE:
 As determined by individual titration (see box warning).
 Usual dosage is 1 or 2 tablets t.i.d. For maintenance, adjust dosage to lowest patient requirement. When necessary, more potent antihypertensives may be added gradually in dosages reduced by at least 50 percent.
HOW SUPPLIED:
 Tablets (dark salmon pink, dry-coated), each containing 0.1 mg reserpine, 25 mg hydralazine hydrochloride, and 16 mg hydrochlorothiazide; bottles of 30, 60, 100 and 1000.
 Consult complete literature before prescribing.

CIBA Pharmaceutical Company
 Division of CIBA-GEIGY Corporation
 Summit, New Jersey 07901

Ser-Ap-Es®

reserpine 0.1 mg
 hydralazine hydrochloride 25 mg
 hydrochlorothiazide 16 mg

...brings three modes of action to bear on hypertension



Thursday, June 9, 1976

See Cadaver Kidney Graft Survival 23% After 5 Years

Continued from page 1

He said he believes it is a valid proposition, and that it is important for physicians, patients, and the community to have a realistic idea of what transplantation can accomplish. He undertook the analysis, Dr. Stubenbord told MEDICAL TRIBUNE, because he felt that no one had taken an objective look at the data heretofore. "Aggregate data from multiple centers suffer from problems of data collection," he noted, "while individual centers may report results on selected groups of patients, thus not giving a representative picture of the status of cadaver transplantation."

While graft survival—defined as function sufficient to not require return to chronic dialysis—has not changed over the past several years, Dr. Stubenbord said, "prominent gains in renal transplantation have been made in enhancing patient survival." Indeed, graft survival does not always imply patient survival; Dr. Stubenbord's analysis showed, in fact, that increased graft survival and increased patient mortality—defined as any mortality following transplantation, regardless of whether the patient had a functioning graft or not—were positively correlated.

So while it is "unlikely that graft survival will increase within the next five years with present therapy," he said, "it is likely that patient survival will gradually improve throughout the country as graft survival is deemphasized." This "de-emphasis," Dr. Stubenbord told MEDICAL TRIBUNE, can take the form, for example, of sacrificing grafts when necessary. "Rather than risking a patient's life by continuing to treat rejected grafts," he said, "we now might choose to simply remove the transplanted kidney."

Dr. Stubenbord went on to say that "there are unquestionably large numbers of patients who have benefited

from transplantation and this benefit has also decreased costs of end-stage renal disease—directly, by eliminating the need for dialysis, and indirectly, by restoring the patients to a more productive life."

Eventually the biologic problems of transplantation will be solved, he continued, but "in the meantime we must plan realistically for the care of all patients with chronic renal failure."

Dr. Stubenbord noted that selecting out certain groups of patients can alter results appreciably. Young, non-diabetic, well-matched, non-responders, for example, have excellent results. "But the problem facing nephrologists is to offer their patients all the possible alternatives. Since we still cannot predict success or failure on an individual basis, there is always a possibility that a graft in a poor risk patient will succeed. The decision to go ahead with such a procedure must depend on a low mortality rate and an informed decision by the patient."

Quality of Life

"The quality of a patient's life can only be determined by the patient himself. A 20% chance of success may be acceptable to some poor risk patients and not to others."

The cases Dr. Stubenbord examined consisted of 280 patients who had received 326 cadaver kidneys (40 patients had two transplants and three patients had three).

Patients with diabetes, cardiovascu-

lar disease, systemic lupus, scleroderma, or malignancy were all part of the population; only patients with fever or infection were excluded.

Great variations could be seen when the patients were examined by groups—such as those who were lympho cytotoxicity positive or negative, or those who were under 40 compared with those who were over 40, (cytotoxicity was measured by screening a panel of lymphocytes from 20 selected donors representing 40 different antigens. Positive cytotoxicity was defined as more than 20% killing of the panel over control levels.) The overall data showed a 40% one-year graft survival with a 13% yearly graft loss thereafter, and a 10% patient mortality the first year with a 2% a year mortality after that.

Those were the figures he used, he explained, to arrive at his projections.



Percodan® Tablets
 4 mg oxycodone HCl (Narcotic)
 650 mg aspirin (Analgesic)
 100 mg phenobarbital (Sedative)
 100 mg promethazine (Antihistamine)

- rapid acting
- effective, reliable oral analgesia in moderate to moderately severe pain
- oxycodone, the principal ingredient of Percodan® is one of the more readily absorbed narcotic analgesics
- one tablet q. 6 h.

Whenver an APC/narcotic is indicated.

Boon to Infection-Prone



Bacteriological isolation suit, designed by Arthur D. Little, Inc., enables patients with defective immune systems to leave laminar-air-flow rooms for specialized treatment while hospital, recreation, or visits with their families.

DESCRIPTION: Each tablet contains 4 mg oxycodone HCl (Narcotic) and 650 mg aspirin (Analgesic) and 100 mg phenobarbital (Sedative) and 100 mg promethazine (Antihistamine). The oxycodone HCl is a potent narcotic analgesic. The aspirin is a potent analgesic and antipyretic. The phenobarbital is a potent sedative. The promethazine is a potent antihistamine.

INDICATIONS: Moderate to moderately severe pain.

CONTRAINDICATIONS: Hypersensitivity to oxycodone HCl, aspirin, phenobarbital, or promethazine.

WARNINGS: Drug Dependence: Oxycodone HCl is a potent narcotic analgesic and may cause physical dependence. Withdrawal symptoms may occur if the drug is discontinued abruptly. The patient should be warned of this possibility and advised to take the drug only as directed.

ADVERSE REACTIONS: The most frequently observed adverse reactions are drowsiness, dizziness, nausea, vomiting, constipation, and dry mouth. Other adverse reactions include hypotension, respiratory depression, and allergic reactions. Some of these adverse reactions may be relieved by the administration of appropriate antidotes.

DOSEAGE AND ADMINISTRATION: Dosage should be adjusted according to the severity of the pain and the response of the patient. The usual adult dose is 1 to 2 tablets every 4 to 6 hours as needed. The usual adult dose is 1 to 2 tablets every 4 to 6 hours as needed.

PRECAUTIONS: Head injury and increased intracranial pressure: The oxycodone HCl may increase intracranial pressure and should be used with caution in patients with head injury or increased intracranial pressure. The patient should be watched for signs of increased intracranial pressure, such as headache, vomiting, and papilloedema.

RESPIRATORY DEPRESSION: Oxycodone HCl may cause respiratory depression. The patient should be watched for signs of respiratory depression, such as shallow breathing, cyanosis, and loss of consciousness. If respiratory depression occurs, the patient should be given oxygen and artificial respiration should be instituted.

ALLERGIC REACTIONS: Allergic reactions to the ingredients of Percodan may occur. Signs and symptoms of allergic reactions include skin rash, hives, and anaphylaxis. If an allergic reaction occurs, the patient should be given appropriate antihistamines and other supportive therapy.

LABORATORY TESTS: Oxycodone HCl may interfere with certain laboratory tests. The patient should be warned of this possibility and advised to inform the laboratory of the use of Percodan.

USE IN PREGNANCY: Oxycodone HCl is a potent narcotic analgesic and may cause fetal harm. The patient should be warned of this possibility and advised to avoid pregnancy while taking Percodan.

USE IN LACTATION: Oxycodone HCl is excreted in breast milk. The patient should be warned of this possibility and advised to avoid nursing while taking Percodan.

OVERDOSE: Overdose of Percodan may cause respiratory depression, hypotension, and loss of consciousness. If overdose occurs, the patient should be given oxygen and artificial respiration should be instituted. The patient should also be given other supportive therapy as needed.

HOW SUPPLIED: Percodan is supplied in the form of tablets. Each tablet contains 4 mg oxycodone HCl, 650 mg aspirin, 100 mg phenobarbital, and 100 mg promethazine.

depression (a decrease in respiratory rate and tidal volume). Chyng-Sha's respiratory system, extreme somnolence, prostration to sleep or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe cases, respiratory depression may lead to death. The onset of very large amounts of death may occur. The onset of very large amounts of death may occur. The onset of very large amounts of death may occur.

PRECAUTIONS: Primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The patient should be watched for signs of respiratory depression, such as shallow breathing, cyanosis, and loss of consciousness. If respiratory depression occurs, the patient should be given oxygen and artificial respiration should be instituted.

ADVERSE REACTIONS: The most frequently observed adverse reactions are drowsiness, dizziness, nausea, vomiting, constipation, and dry mouth. Other adverse reactions include hypotension, respiratory depression, and allergic reactions. Some of these adverse reactions may be relieved by the administration of appropriate antidotes.

DOSEAGE AND ADMINISTRATION: Dosage should be adjusted according to the severity of the pain and the response of the patient. The usual adult dose is 1 to 2 tablets every 4 to 6 hours as needed. The usual adult dose is 1 to 2 tablets every 4 to 6 hours as needed.

PRECAUTIONS: Head injury and increased intracranial pressure: The oxycodone HCl may increase intracranial pressure and should be used with caution in patients with head injury or increased intracranial pressure. The patient should be watched for signs of increased intracranial pressure, such as headache, vomiting, and papilloedema.

RESPIRATORY DEPRESSION: Oxycodone HCl may cause respiratory depression. The patient should be watched for signs of respiratory depression, such as shallow breathing, cyanosis, and loss of consciousness. If respiratory depression occurs, the patient should be given oxygen and artificial respiration should be instituted.

ALLERGIC REACTIONS: Allergic reactions to the ingredients of Percodan may occur. Signs and symptoms of allergic reactions include skin rash, hives, and anaphylaxis. If an allergic reaction occurs, the patient should be given appropriate antihistamines and other supportive therapy.

LABORATORY TESTS: Oxycodone HCl may interfere with certain laboratory tests. The patient should be warned of this possibility and advised to inform the laboratory of the use of Percodan.

USE IN PREGNANCY: Oxycodone HCl is a potent narcotic analgesic and may cause fetal harm. The patient should be warned of this possibility and advised to avoid pregnancy while taking Percodan.

USE IN LACTATION: Oxycodone HCl is excreted in breast milk. The patient should be warned of this possibility and advised to avoid nursing while taking Percodan.

OVERDOSE: Overdose of Percodan may cause respiratory depression, hypotension, and loss of consciousness. If overdose occurs, the patient should be given oxygen and artificial respiration should be instituted. The patient should also be given other supportive therapy as needed.

HOW SUPPLIED: Percodan is supplied in the form of tablets. Each tablet contains 4 mg oxycodone HCl, 650 mg aspirin, 100 mg phenobarbital, and 100 mg promethazine.

Endo Inc.
 Manual, Puerto Rico 00701
 Subsidiary of E.I. du Pont de Nemours & Co. (Inc.)
 EDO 8750

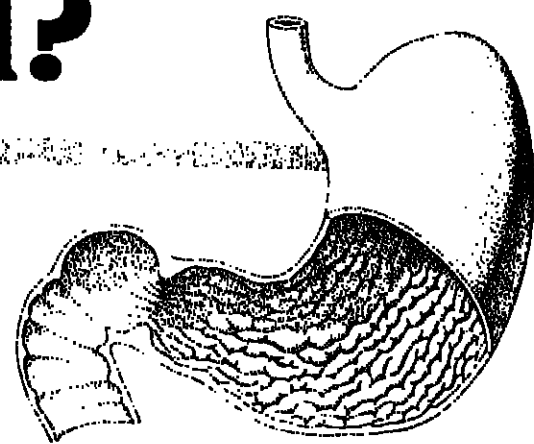
20 mg to a maximum of 200 mg.
RANDOLPH PHARMACEUTICALS, EAST HANOVER, NEW JERSEY 07936

Duodenal Ulcer*...Irritable Bowel*

Are these patients getting all the symptomatic relief they need?

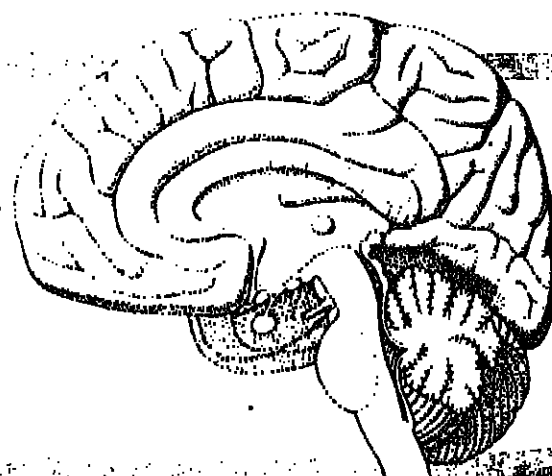
Some medications reduce spasm but not gastric hypersecretion...

Librax reduces both



Some medications reduce secretory and spasmodic symptoms but do not relieve associated anxiety...

Librax does both



Librax reduces both emotional and somatic factors with the economy and convenience of a single medication...all advantages in sustaining patient compliance.

adjunctive **Librax**® a distinctive antianxiety-anticholinergic agent

Each capsule contains 5 mg chloridazepoxide HCl and 2.5 mg cildinium Br.

Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chloridazepoxide hydrochloride and/or cildinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium® (chloridazepoxide hydrochloride) to known addicts.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or gradually as needed and tolerated. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacologic effects of agents, particularly potentiating drugs, such as MAO inhibitors and renal or hepatic function. Paradoxical reactions (e.g., excitement, agitation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations have been reported with either compound alone have been reported with Librax. chloridazepoxide hydrochloride is used alone, drowsiness, confusion and confusion may occur, especially in the elderly and debilitated. These are avoidable in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also reported are isolated instances of skin eruptions, edema, menstrual irregularities, nausea and constipation, orthostatic hypotension, increased and decreased libido—all infrequent symptoms, generally controlled with dosage reduction, changes in EEG patterns (low-voltage fast activity) may appear during and after treatment. blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chloridazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Wednesday, June 9, 1976

The Only Independent Weekly Medical Newspaper in the U.S.

Medical Tribune

and Medical News
Published by Medical Tribune, Inc.

Drug Perspectives and Policy Need Reason, Not Rhetoric

TOO MANY of our orientations, legal, medical and social, are related to widely propagated, popular mythology. Our attitude towards psychotropic agents such as marijuana is a classic case in point. In Current Opinion (page 20), one of our country's foremost experts on abuse of drugs makes a number of points of importance to every practicing physician and patient in debunking marijuana mythology:

Continuous users of marijuana may number as little as one-tenth that of regular users of alcohol. One hundred million Americans use alcohol regularly; only 13 million, out of 32 million who have experimented with marijuana, use it more than once.

As to violence, marijuana, popular with the "flower children" of the past, is rejected by militant groups because, by inducing peaceful attitudes, it may distract from activist change or revolution.

As to the stepping-stone theory that marijuana leads to hard drug addiction, it is noted that "virtually every study has shown that alcohol and nicotine are the initial drugs of experimentation by our heroin addicts (95% have used alcohol) and everyone else as well."

As to the "amotivational syndrome" (the exact opposite of the "hashish violence" mythology), longitudinal studies have shown no detriment to motivation as measured by school performance.

As to brain damage, a single report of ventriculogram studies has not been

confirmed; neither has a single report on effects on the body's immune mechanisms.

It would seem that social and political policy has played a major role in public and police attitudes towards psychoactive drugs. A report of the National Commission on Marijuana, and Drug Abuse, of which Dr. Ungerleider was a member, represented a massive, non-political and non-moral, scientific and social effort to get at the truth about marijuana. If marijuana is a health problem, the extent should be determined scientifically.

Since great hullabaloes are raised with one, five, or 50 avoidable deaths resulting from therapeutic agents, one is moved to wonder at the political and press silence when a single psychoactive recreational drug, such as alcohol, used for social purposes, is involved in "35,000 traffic fatalities, one million traffic accidents, and one half of all violent crimes" in the U.S. each year.

The test of probity in respect to the public health would seem to be the willingness of political and social leaders to seek actions proportioned to problems in areas of public health. It would seem, according to Dr. Ungerleider, that in respect to marijuana, "medicine seems to be returning to science, politicians to truth, and the public to sanity." It is to be hoped that such new attitudes will become more widespread with respect to drugs generally. Reason must displace rhetoric for proper drug perspectives and health policies.

A.M.S.

The Nutrition Gap...

THE NUTRITION GAP, between what is known and what is being medically conveyed, widens. It is difficult to understand the continuing neglect of this vital subject in the medical curriculum.

Further, as a result of medical default the public is increasingly de-

pendent for nutritional information on non-medical sources. Lay publications, particularly women's magazines, and a number of health periodicals have done fair to creditable jobs, but much too much of this field has been pre-empted by faddists and irresponsible exploiters of public ignorance.

...And The Pregnant Woman

PARTICULARLY DISTURBING is the medical failure to put into practice important findings in the field of maternal nutrition. The early reports of M. B. Strauss (*Am. J. Med. Sci.* 190:811, 1935) and Robert A. Ross (*South. Med. J.* 28:120, 1935) on the relationship of nutrition to eclampsia or convulsive metabolic toxemia of late pregnancy have been landmark investigations. Dr. Tom Brewer, who has referred to these pioneers time and

again, has demonstrated with his own findings that proper nutrition has resulted in a marked reduction in the incidence of eclampsia or convulsive MTLP in practice. His observations are concordant with those of Hamlin in Australia (*Lancet* 1:64, 1952). The findings have been consistent for almost 40 years. One would expect in so tender an area as maternal and fetal health a greater sense of urgency.

A.M.S.

Pneumococcal Vaccine

CLINICAL QUOTE: "Were the number of antigens in the vaccine to be increased... and the vaccine to be used widely, the prospect of largely eliminating the half million pneumo-

coccal pneumonias estimated to occur annually in the adult population of this country would appear...realizable." (Dr. Robert Austrian, of the University of Pennsylvania. See page 1.)



"Why do you keep coming out with new diseases—before you cure the old ones?"

© 1976, Medical Tribune, Inc.

LETTERS TO TRIBUNE

On Tuberculosis Therapy

The report of my remarks [on short-term therapy for tuberculosis] at the Pulmonary Disease Symposium at the New York Academy of Medicine (MT, April 21) is, in general, well done. Unfortunately, no mention was made of the Public Health Service's TB Control Division, which is coordinating the controlled trials; and I do not believe I said that pregnancy is a contraindication to preventive therapy—it is not contraindicated, but prudent to delay until after delivery.

PHYLIS Q. EDWARDS, M.D.
Indian Health Service
Training Center
Tucson, Ariz.

The Good Drugs Do

Encore! Encore! Regarding your excellent education pullout (*The Good Drugs Do*, MT, March 10) under Dr. Lassagna's editorship; patients have a way of carrying off such items too soon for all to benefit.

Strongly suggest you supply these either: 1) in duplicate or 2) supply them with a jacket cover large enough to accumulate them, (a clear plastic cover would do), 3) offer them for sale by the dozen for patient handouts, or 4) some combination of the previous 3.

R. D. LAUSA, M.D.
Columbus, O.

An "Informed" Consent

Being deeply involved in medicolegal matters, particularly as an educator, I was extremely interested in Mr. Nathan Horwitz' article, on "Informed Consent Study" (MT, Feb. 26). Having practiced internal medicine for over 30 years, I can attest to the findings of Dr. George Robinson, the author of the study.

However, in retrospect, I wonder how adequate and appropriate was the information that I and Dr. Robinson gave our patients. This is one of the questions to be answered in evaluating Dr. Robinson's data. He assumes, as I and all other physicians do, that we decide what, how, when and where is appropriate for the patient. We must remember, that the test for the adequacy

of "informed consent" is subjective—not objective. It is what a particular patient needs to know in making an enlightened and knowledgeable decision. It is not what we physicians choose to tell in the manner and forum that we select. I do not write this letter in criticism of Dr. Robinson's study, but merely to test his and other physicians' conclusions about the concept of "informed consent."

HAROLD L. HIRSCH, M.D., J.D.,
F.C.L.M.
Washington, D.C.

Second Opinions

In evaluating the validity of the Blue Cross "second opinion" [MT, April 7], I would like to call attention to what I refer to as the "Professor Syndrome."

As a young ob-gyn physician in the early days of my practice, I often would suggest surgery to one of my patients; only to have her go to a "professor," who upon examining my patient, would inform her that the surgery "was unnecessary."

To my dismay, usually on the return visit to the "professor," the surgery then became urgent, and was subsequently performed by the professor.

Blue Cross should be advised that their statistics had best be held in abeyance until they have at least one year's experience. It is very possible that what was not initially necessary may have become necessary but with a different operative physician!

DAVID PLOTKIN, M.D.
(Older and wiser)
Massapequa, N.Y.

Unjustified Surgery?

Your editorial, "Abuse of the Press and Science" (MT, Mar. 17), was very accurate and informative. Your readers might be interested in "Unjustified Surgery—Fact or Myth?", which I wrote (*N.Y. State J. Med.* 76:454, Mar., 1976). It emphasizes the issue of abuse referred to in your editorial.

RALPH S. EMERSON, M.D.
President
Medical Society of
State of New York
Lake Success, N.Y.

Valium® (diazepam) has a range of clinical applications no other benzodiazepine can match

ROCHE

Indicated in anxiety, psychic tension and psychoneurotic anxiety with secondary depressive symptoms

A number of benzodiazepines can be used for treating anxiety. But Valium is the only one specifically indicated in such a wide range of situations where anxiety is clinically significant. For example, I.M. Valium is specifically indicated for anxiety prior to surgery. I.V. Valium is specifically indicated prior to elective cardioversion and as an adjunct prior to endoscopic procedures... and, it provides the added benefit of diminished patient-recall in these situations. When used orally as a psychotherapeutic agent, Valium is specifically beneficial for the muscular tension and other somatic and psychic symptoms of anxiety. And, it may also be used when psychoneurotic anxiety is accompanied by secondary depressive symptoms. It all comes down to this: *Valium—the benzodiazepine you know and trust—gives you a broader range of clinical utility than any other benzodiazepine.* And because adverse reactions more serious than drowsiness, fatigue and ataxia are rare, Valium is relatively safe. Do, however, caution patients against driving, operating dangerous machinery or the simultaneous drinking of alcohol. Also encourage patients to adhere to the prescribed dosage regimen or to discuss any needed adjustment with you.

Indicated adjunctively in skeletal muscle spasm and certain spastic disorders

Valium (diazepam) is the only benzodiazepine indicated in skeletal muscle spasm and spasticity. And here, too, its indications are extensive and quite specific: as an adjunct in skeletal muscle spasm due to reflex spasm to local pathology such as herniated disc or acute muscle strain; adjunctively in spasticity associated with paraplegia; adjunctively in spasticity due to cerebral palsy and athetosis; adjunctively in stiff-man syndrome and tetanus (the parenteral route only is used in tetanus).

Valium can break the spasm/pain/spasm cycle, bringing more comfort and mobility to the patient with low-back syndrome. Valium can reduce involuntary movements, bringing more confidence and a boost in morale to patients with upper motor neuron disorders. It's the one benzodiazepine with clinically proven muscle-relaxant activity.

Indicated adjunctively in certain convulsive disorders



As an anticonvulsant, the clinical applications of Valium (diazepam) even extend to life-threatening situations. Injectable Valium administered intravenously is preferred in status epilepticus and severe recurrent seizures. Among the reasons: its effectiveness, speed of action, duration of seizure control and relative safety. Oral Valium has also been used as an adjunct in certain minor motor seizures, but has not been proved useful as sole therapy.

Whenever Injectable Valium is used I.V., it should be injected slowly, at least one minute for each 5 mg (1 ml) given. Avoid small veins, i.e., on the dorsum of the hand or wrist, as well as intra-arterial administration or extravasation. Injectable Valium should not be mixed or diluted with other solutions or drugs and should not be added to I.V. fluids.

2-mg, 5-mg, 10-mg scored tablets
2-ml Tel-E-Ject® disposable syringes
2-ml ampuls
10-ml vials } 5mg/ml

Valium®^{IV}
(diazepam)
One of a kind.

Please turn page for a summary of product information.

Vicki Morrison Administration Manager
Isabel Hutchings Conference Manager
Charlotte Benton-Hughes Conference Manager
Kerry Brown Technical Services Manager

Surrey TW20 2LS
Tel: 081 332 2422
Fax: 081 332 0939

Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets
2-ml Tel-E-Ject® disposable syringes
2-ml ampuls } 5mg/ml
10-ml vials }

- the one benzodiazepine with three clinically useful pharmacologic properties
- a range of clinical applications unmatched by any other benzodiazepine
- dosage flexibility no other benzodiazepine can match
- a distinct pharmacokinetic profile that includes diazepam and three active metabolites

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, impending or acute delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in: relief of skeletal muscle spasm due to reflex spasm to local pathology; spastically caused by upper motor neuron disorders; athetosis; stiff-man syndrome. *Oral form* may be used adjunctively in convulsive disorders, but not as sole therapy. *Injectable form* may also be used adjunctively in: status epilepticus; severe recurrent seizures; tetanus; anxiety, tension or acute stress reactions prior to endoscopic and surgical procedures; cardiovascular.

Contraindications: Use of injectable in infants and Tablets in children under 6 months of age; known hypersensitivity to drug; acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: As with most CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Advise patients against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals (drug addicts or alcoholics) under careful surveillance because of their predisposition to habituation and dependence. Use of any drug in pregnancy, nursing women or in women of childbearing potential requires that expected benefit be weighed against possible hazard.

ORAL: Not of value in treatment of psychotic patients; should not be employed in lieu of appropriate treatment. When using oral form adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increase in dosage of standard anticonvulsant medication; abrupt withdrawal in such cases may also be associated with temporary increase in frequency and/or severity of seizures.

INJECTABLE: When used I.V., the following procedures should be undertaken to reduce the possibility of venous thrombosis, phlebitis, local irritation, swelling, and, rarely, vascular impairment. Inject slowly, taking at least one minute for each 5 mg (1 ml) given; do not use small veins, i.e., dorsum of hand or wrist; extreme care should be taken to avoid intra-arterial administration or extravasation. Do not mix or dilute with other solutions or drugs; do not add to I.V. fluids.

Administer with extreme care to elderly or very ill and those with limited pulmonary reserve because of possibility of apnea and/or cardiac arrest; resuscitative facilities should be available. When used with narcotic analgesic, eliminate or reduce narcotic dosage at least 1/2 and administer in small increments. Not recommended for OB use until additional information is available. Should not be administered to patients in shock, coma or in acute alcoholic intoxication with depression of vital signs.

Precautions: If combined with other psychotropics or anticonvulsants, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium (diazepam), such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants. Protective measures indicated in highly anxious patients with accompanying depression who may have suicidal tendencies. Observe usual precautions in impaired hepatic function; avoid accumulation in patients with compromised kidney function. Limit oral dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation (Initially 2 to 2 1/2 mg once or twice daily, increasing gradually as needed or tolerated).

INJECTABLE: Laryngospasm and increased cough reflex are possible during peroral endoscopic procedures; use topical anesthetic and have necessary countermeasures available; hypotension or muscular weakness possible, particularly when used with narcotics, barbiturates or alcohol. Use lower doses (2 to 5 mg) for elderly and debilitated; safety

and efficacy in children under 12 not established.

Adverse Reactions: Side effects most commonly reported were drowsiness, fatigue and ataxia. Infrequently encountered were confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo and blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, use of the drug should be discontinued.

Because of isolated reports of neutropenia and jaundice, periodic blood counts and liver function tests are advisable during long-term therapy. Minor changes in EEG patterns, usually low-voltage fast activity, have been observed in patients during and after Valium (diazepam) therapy and are of no known significance.

INJECTABLE: Venous thrombosis and phlebitis at injection site, hypotension, syncope, bradycardia, cardiovascular collapse, nystagmus, urticaria, hiccups, neutropenia.

In peroral endoscopic procedures, coughing, depressed respiration, dyspnea, hyperventilation, laryngospasm and pain in throat or chest have been reported.

Dosage: Individualized for maximum beneficial effect.

ORAL—Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; acute alcohol withdrawal, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2 1/2 mg 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2 1/2 mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

INJECTABLE: Usual initial adult dose is 2 to 20 mg I.M. or I.V., depending on indication and severity. Larger doses may be required in some conditions (tetanus). In acute conditions injection may be repeated within 1 hour, although interval of 3 to 4 hours is usually satisfactory. Lower doses (usually 2 to 5 mg) with slow dosage increase for elderly or debilitated patients and when sedative drugs are added. (See Warnings and Adverse Reactions.)

I.M. use: by deep injection into the muscle.

I.V. use: inject slowly, take at least one minute for each 5 mg (1 ml) given. Do not use small veins, i.e., dorsum of hand or wrist. Use extreme care to avoid intra-arterial administration or extravasation. Do not mix or dilute with other solutions or drugs; do not add to I.V. fluids. Moderate psychoneurotic reactions, 2 to 5 mg I.M. or I.V. and severe psychoneurotic reactions, 5 to 10 mg I.M. or I.V., repeat in 3 to 4 hours if necessary; acute alcoholic withdrawal, 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours if necessary; muscle spasm, 5 to 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours if necessary (tetanus may require larger doses); status epilepticus, severe recurrent convulsive seizures, 5 to 10 mg I.M. or I.V. initially, repeat in 2 to 4 hours if necessary. In endoscopic procedures, titrate I.V. dosage to desired sedative response, generally 10 mg or less but up to 20 mg (if narcotics are omitted) immediately prior to procedure; if I.V. cannot be used, 5 to 10 mg I.M. approximately 30 minutes prior to procedure. As preoperative medication, 10 mg I.M.; in cardioversion, 5 to 15 mg I.V. within 5 to 10 minutes prior to procedure. Once acute symptomatology has been properly controlled with injectable form, patient may be placed on oral form if further treatment is required.

Management of Overdosage: Manifestations include somnolence, confusion, coma and diminished reflexes. Monitor respiration, pulse, blood pressure; employ general supportive measures, I.V. fluids, adequate airway. Immediate gastric lavage indicated for overdosage with tablets. Use levaterenol or metaraminol for hypotension, caffeine and sodium benzoate for CNS-depressive effects. Dialysis is of limited value.

Supplied: Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose® (unit dose) packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10. Ampuls, 2 ml, boxes of 10; Vials, 10 ml, boxes of 1; Tel-E-Ject® (disposable syringes), 2 ml, boxes of 10. Each ml contains 5 mg diazepam, compounded with 40% propylene glycol, 10% ethyl alcohol, 5% sodium benzoate and benzoic acid as buffers, and 1.5% benzyl alcohol as preservative.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Monday, June 9, 1976

MEDICAL TRIBUNE

15

Bell's Palsy: A Virus-Caused Form of Cranial Polyneuritis?

Continued from page 1

new and somewhat controversial concept of Bell's palsy. Dr. Adour himself had the disease.

Traditionally, Bell's palsy has been an idiopathic term for facial paralysis of unknown cause, according to Dr. Adour. It has been thought of as an acute, unilateral disease of the intracranial portion of the seventh cranial nerve, that is, the facial nerve.

This is now in dispute. After studying over 1,000 patients, Dr. Adour is convinced that the paralytic process began as a herpes simplex infection of the seventh cranial nerve which then moves on to the seventh.

Multiple Nerve Involvement

A neurological exam reveals multiple nerve involvement. In our series, 27% of patients had hypesthesia of one or more branches of the trigeminal nerve, 3% had motor involvement with weakness of the masseter or pterygoid muscle, 43% have abnormal electroencephalograms of the vestibular nerve, 2% had hyperacusis of the cochlear nerve, and 35% had hypesthesia of the sympathetic nerve.

Furthermore, examination of the tongue reveals that the "fungiform papillae" are inflamed not only on the affected side, but also on the clinically unaffected side," Dr. Adour notes.

Dr. Robert E. Lovelace, director of the Electromyography and Nerve Conduction Laboratories at Columbia's Neurological Institute remarks, "We are faced with a truly interesting concept here. We appear to be seeing only the tip of the iceberg in Bell's palsy."

Although conclusive evidence is lacking, researchers are investigating a link to the disease. Virus titers run on 41 patients in a controlled revealed herpes simplex as the only virus in serum. Dr. Adour says. He notes that herpes simplex inoculated into animals has reproduced the disease.

Dr. Adour believes the virus gains a foothold in the respiratory tract, travels by the axons of the sensory nerves to sensory ganglions where it remains dormant until reactivated.

"Minor epidemics of Bell's palsy have been observed at times when herpes simplex activity is high," he says.

Females aged 10 to 19 develop the disease twice as often as males the same age, according to Dr. Adour. Onset is usually within the first 14 days of the menstrual cycle. "Body temperature goes up and the virus is activated," he explains. Pregnant women are three to four times as likely as nonpregnant women to contract Bell's palsy and six times more likely to do so in the third trimester, he says.

Presenting symptoms are excessive tearing, numbness in the face, pain behind the ear, abnormal taste sensation and sensitivity to loud noises.

The test, which occurs in almost 50% of cases, must be distinguished from hearing loss. "Any patient with hearing loss should be immediately referred to an otolaryngologist. Hearing loss is not associated with Bell's palsy," Dr. Adour stresses.

Steroid therapy is recommended;

surgical decompression is not. "Prednisone does not affect the course of the disease but protects the nerve from allergic or autoimmune inflammatory reactions," says Dr. Adour. For adults the dosage is 30 mg b.i.d. for the first five days.

The patient should be sent within the first three days to the hospital for nerve excitability tests. If test results are abnormal, then the prednisone is continued for another 11 days. Dosage is then tapered to zero over the next five days.

"Prednisone should not be discontinued abruptly even if vesicles appear in the ear after treatment is begun. This

represents normal progression of the disease, not a drug reaction," Dr. Adour emphasizes. "A maximum of 21 days treatment is recommended since this covers the acute phase of the disease."

Uncomplicated recovery takes three to six weeks but all patients should improve within three to six months. "If they don't, then it's not Bell's palsy," Dr. Adour notes. "One thing physicians should be very aware of is that patients tend to become very depressed in the second week. They need a little extra attention then but no antidepressants."

94% of Treated Recover

All patients should be treated although diabetics, hypertensives and psychoneurotics are high risk patients, Dr. Adour says. "If untreated, 80% of patients will recover completely, but

we can't predict which. When treated, 94% of patients recover. Only 6% do badly although some recovery is evident."

Early referral of all patients with suspected Bell's palsy to a facial nerve diagnostic and treatment center is urged by both Drs. Lovelace and Adour. "The steroid regime is still so relatively new and the effect of the disease so devastating if good results are not obtained," Dr. Lovelace told MEDICAL TRIBUNE, "that referral cannot be too strongly emphasized."

Steroids are more likely to be effective if treatment is begun within three days of onset of symptoms, he said. Indeed, treatment begun later than the fifth day is apt to be less effective, and after two weeks any benefit from steroid therapy is doubtful, the New York investigator emphasized.

ONE TWO THREE SIMPLE STEPS TO REMOVE EAR WAX

UNIQUE CERUMENOLYTIC

Fill external canal with the drops, with patient's head tilted at 45° angle;

Insert cotton plug and allow to remain for only 15 to 30 minutes;

Remove plug and gently wash ear with lukewarm water, using soft rubber syringe.

SIMPLE 15-30 MINUTE HOME OR OFFICE PROCEDURE WITHOUT INSTRUMENTATION

- Clears the ears prior to ear examination, otologic therapy or audiometry.
- Specific cerumenolytic action—excellent results reported in over 90% of 2,700 adult and pediatric patients.*
- Needs no repeated installations for several days, unlike some other agents.

Indications: Removal of cerumen; removal of impacted cerumen prior to ear examination, otologic therapy or audiometry. **Contraindications:** Previous untoward reaction to the drops; positive patch test. **Precautions:** Patch

test in patients with suspected or known allergy. Use with caution in otitis externa; avoid using in otitis media, presence of perforated drum, known dermatologic sensitivity or other allergic manifestations. Avoid undue exposure of large skin areas to the drug. **Adverse Reactions:** Reported incidence in clinical studies* is about 1%, ranging from mild erythema to severe exfoliative reaction of external ear and periauricular tissue; all reported uneventful resolution and no sequelae. *Bibliography and detailed information available upon request. **Purdue Frederick**

© COPYRIGHT 1974, 1976, THE PURDUE FREDERICK COMPANY/INDIANAPOLIS, INDIANA 46206

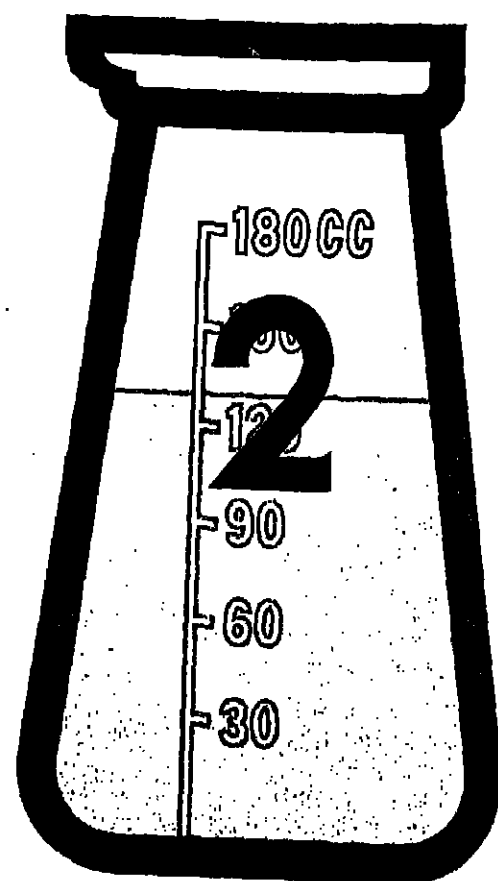
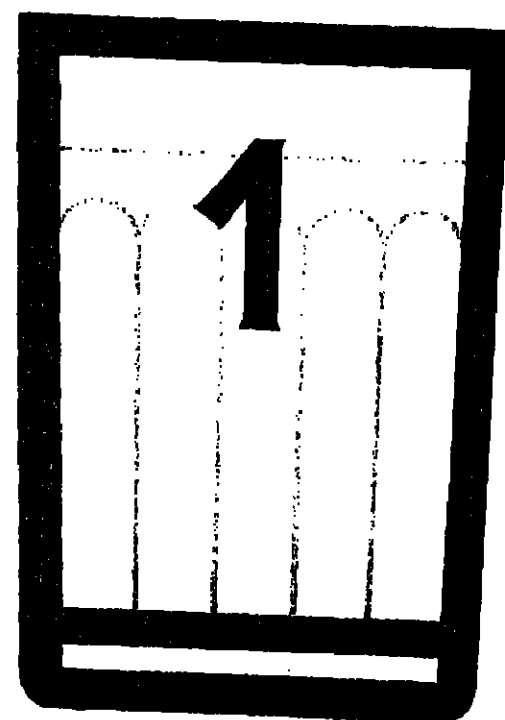
CERUMENEX DROPS

(triethanolamine polypeptide oleate condensate 100% in propylene glycol with chlorbutanol 0.5%)

Rx for Home and/or Office Use

Vicki Morrison Administration Manager
Isabel Hutchings Conference Manager
Charlotte Benton-Hughes Conference Manager
Kerry Brown Technical Services Manager

Tel: 081 332 2422
Fax: 081 332 0939



The 3rd Basic

Adequate fluid intake

Frequent voiding

Gantanol (sulfamethoxazole) B.I.D.

4 tablets (0.5 Gm each) STAT—then 2 tablets B.I.D. for 10-14 days

Basic therapy with convenience for acute nonobstructed cystitis

• Effective against susceptible *E. coli*, *Klebsiella*, *Aerobacter*, *Staph. aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms.

Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterialia including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical

signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, methemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, lacy lesions, pruritus, exfoliative dermatitis, anaphylactic reactions, periorbital edema, conjunctivitis and scleritis); gastrointestinal reactions (nausea, vomiting, abdominal pain, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); CNS reactions (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); miscellaneous reactions (drug fever, chills, toxic nephrosis with oliguria and anuria, periarthritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some glycosides, acetazolamide, thiazides and oral hypoglycemics, sulfonamides have caused hypoglycemia as well as thyroid malfunctions in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis). Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm b.i.d. or t.i.d. depending on severity of infection. Usual child's dosage: 0.5 Gm (1 tab or teasp.) 120 lbs of body weight initially, then 0.25 Gm/kg/24 hrs. Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

ROCHE Roche Laboratories Division of Hoffman-La Roche Inc. Nutley, New Jersey 07110

INTERNATIONAL REPORT

from Japan from the Editors of Medical Tribune Japan, Tokyo

MDs, Priests, Discuss Life Support of 'Vegetative' Patients

Medical Tribune World Service

TOKYO—Reflecting the concerns felt by physicians world-wide over the continued maintenance of "vegetative" patients through life-support systems, many physicians, lawyers and priests participating in a symposium sponsored by a group of clinicians concluded that euthanasia must be accepted as unavoidable in certain situations. However, others stressed the difficulties, when faced with the reality, in making such a decision.

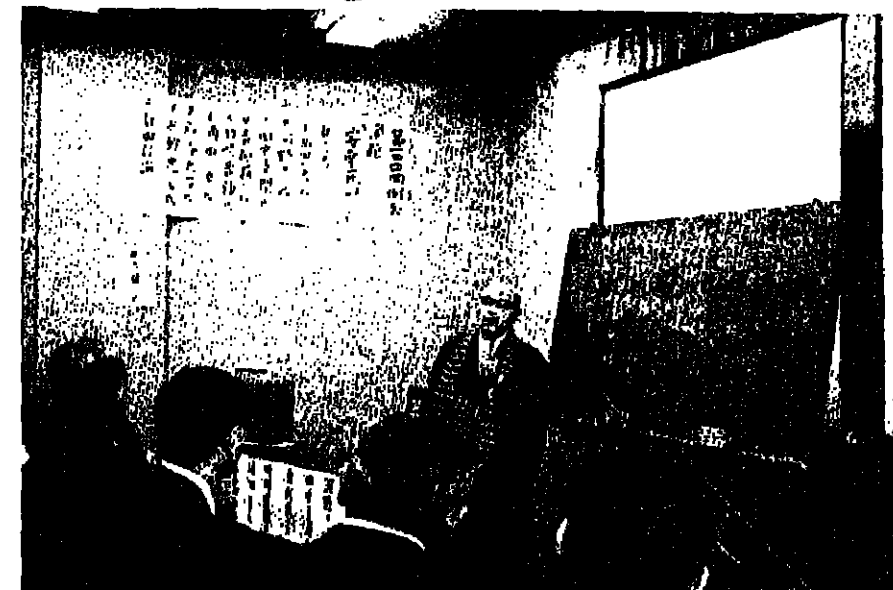
Dr. Rin Kohno, Tokyo Metropolitan Kansatsu Imuin (Supervisory Hospital), pointed out that the presence of a so-called "vegetative" patient creates an almost unbearable stress on the physicians and nurses as well as on the patient's family. Not infrequently, he said, the family, burdened with financial and emotional problems, may be driven into requesting euthanasia for their loved one. The progress of medicine is causing an increase in the

number of patients with serious brain damage who can be kept alive, he said.

A lecturer at the Tokyo Jikeikai Medical College, Dr. Takashi Urata, held that such patients should be classed as alive or not alive, adding that he would consider a patient alive as long as his metabolism was functioning. Yet he also felt that it was most important to take a well-balanced look at the total situation, without limiting it to the patient, and including the welfare of the family, with the final decision being left to the physician's judgment.

"A request for euthanasia," written by the patient while he has the capacity to make a sound judgment, should be considered as valid as a last will and testament, Dr. Urata said.

Many physicians at the symposium classed euthanasia as active or passive and held that the physician should make it a rule to take a passive approach to euthanasia.



At euthanasia symposium, Tokin Tonoya, a priest of Ekakuji Temple, Kamakura, described "senge," a Buddhist concept of an "ideal form of demise," permitted only to a high Buddhist priest who, after he has finished his mission to edify the people of the world, realizes Nirvana. It is said that he can realize exactly when he will die, weeks in advance, and passes away just as if going to sleep.

from Germany from the Editors of Medical Tribune Germany, Wiesbaden

Eliminating Cheese, Other Food Allergens, Relieves Acne

Medical Tribune World Service

ZURICH—A strict elimination diet after systematic intracutaneous testing of about 40 food allergens in 400 patients with acne vulgaris, most of whom were between 20 and 30 years of age, gave surprisingly rapid alleviation of the skin condition. Flare-ups, when they occurred, were due solely to nonadherence to the elimination diet in which

all positive food allergens were omitted, according to Dr. V. Obeld-Ruggli, of Zurich. She reported at the Fifty-Seventh Annual Congress of the Swiss Society for Dermatology and Venerology here. Results in over 70% of the patients were very good to good when the regimen was strictly adhered to.

Although hormonal disorders, bacterial infections and digestive distur-

ances are frequently said to trigger and aggravate common acne, its etiology has not yet been definitely established. In the present investigation, special attention was paid to cheese, vegetables producing flatulence, smoked and pickled meat, spices, puff pastry, confections based on wheat flour, candies, eggs, chocolate, tomatoes and nuts. The greatest number of positive results

corresponded to the cheese test (388 cases), followed by tomatoes (242), mustard and paprika (149), and pepper (125). Nearly all patients presented several positive results; strikingly, however, patients with intensely pustular and nodose forms gave fewer positive test results than the remainder.

After the test results had been ob-

Continued on page 27

from Britain from the Editors of Medical News-Tribune, London

Beta-Blockers Reduce Risk of First-Time Infarcts

Medical Tribune World Service

LONDON—Patients with severe hypertension are less likely to develop a myocardial infarction if the treatment regime includes the use of beta-blockers, says Dr. I. Stewart of the Victoria Hospital, Blackpool.

Dr. Stewart, who spoke at the 4th meeting of the International Society of Hypertension, in Sydney, Australia,

described a study in which 169 patients with essential hypertension were followed up for over five years.

He found that those in whom the treatment regime did not include a beta-blocker were four times more likely to develop a myocardial infarction, other risk factors for myocardial infarction having been standardized where possible.

Beta-blockers have been shown previously to reduce the risk of re-infarction, but to Dr. Stewart's knowledge this is the first study to show that it reduces the risk of first-time infarctions in hypertensive patients.

Hypotensive Agents Also

In many patients with severe hypertension, treatment may have to be started with a quicker acting hypotensive

agent, but in general Dr. Stewart finds it possible to introduce beta-blockers within weeks of onset of therapy.

Not all patients can be given beta-blockers. He has found that in about 25% of patients, some contraindication to beta-blockade is present.

One example of an illness that contraindicates the use of beta-blockers is asthma, Dr. Stewart said.

from France from the Editors of Tribune Medicale, Paris

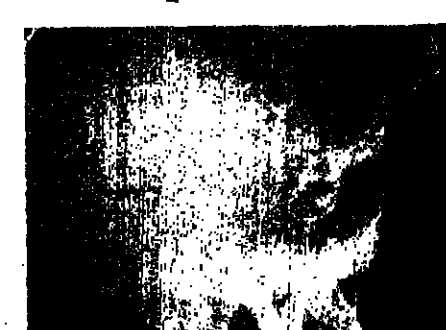
Arteriography Indispensable in Dx of Cerebral Insufficiency

Medical Tribune World Service

LILLE—At a round table discussion of the treatment of insufficiency of cerebral circulation, Professor Marcel Jomin, of the neurosurgery service of the Centre Hospital Universitaire de Lille, and Dr. Gerard Gozet, neuroradiologist at the same hospital, reviewed the examinations that may be used to confirm the diagnosis.

Not all examinations have the same value, Professor Jomin said. He classifies them into three groups:

Useful: 1.) Physical examination of the fundi, ophthalmodynamometry,



Angiography, considered indispensable by Prof. Jomin, showed this patient to have complete occlusion of the right carotid bifurcation.

thermography, electronystagmography and echography; 2.) x-rays of neck and skull may show arterial calcifications. Should there be the slightest question of a cerebral accident, he feels a lumbar puncture should be performed.

Very useful: 1.) Assessment of physical function; 2.) an electroencephalogram.

Indispensable: Arteriography to locate a surgically treatable carotid artery lesion. There is almost always some conflict between a minimal clinical picture and extensive anatomical

damage to the carotid arteries

Arteriography is particularly indicated in a young subject, in case of a syndrome of cerebral carotid claudication, vertebro-basilar or mixed, and when an old syndrome of cerebral circulatory insufficiency, poorly controlled by treatment alone, suddenly flares up. It is usually contraindicated when the patient is over 70 years of age, when his general physical condition is precarious, when there is a permanent neurologic deficit (with dis-

Continued on page 27

Wednesday, June 9, 1976

SANOREX[®] (MAZINDOL) TABLETS, 1 mg and 2 mg

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a pressor amine agent (e.g., levaterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and instituting pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychologic dependence. Manifestations of chronic overdependence or withdrawal with mazindol have not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Usage in Pregnancy: An increase in neonatal mortality and a possible increased incidence of rib anomalies in rats were observed at relatively high doses.

Usage in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdosage. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia. Cardiovascular: Palpitation, tachycardia. Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, drowsiness, weakness. Gastrointestinal: Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. Skin: Rash, excessive sweating, clamminess. Endocrine: Impotence, changes in libido, have rarely been observed. Eyes: Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: 1 mg, three times daily, one hour before meals, or 2 mg, once daily, one hour before lunch. The lowest effective dose should be used. Should GI discomfort occur, mazindol may be taken with meals.

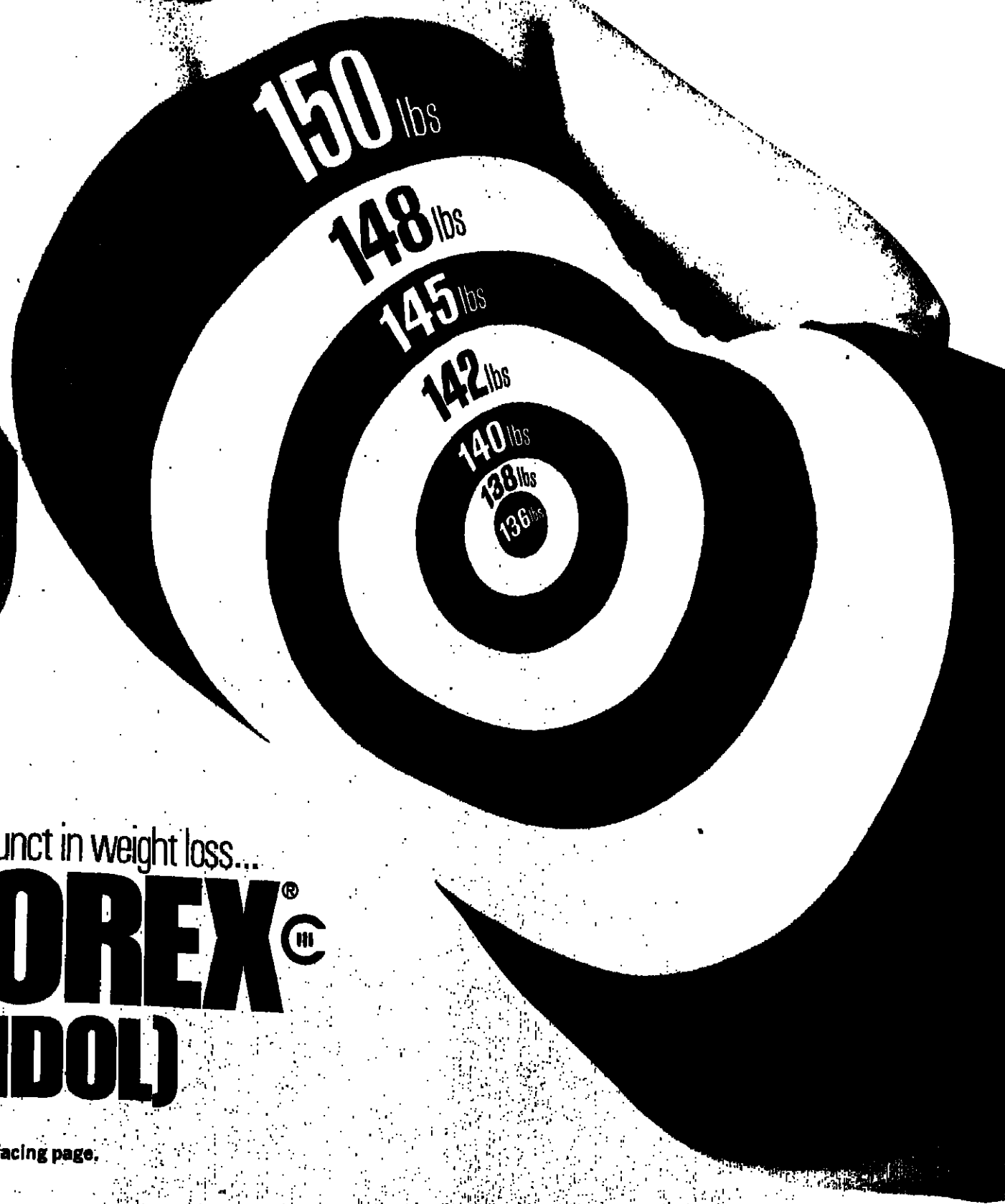
Overdosage: There are no data as yet on acute overdosage with mazindol in humans. Manifestations of acute overdosage with amphetamines and related substances include restlessness, tremor, rapid respiration, dizziness, fatigue and depression may follow the stimulatory phase of overdosage. Cardiovascular effects include tachycardia, hypertension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting and abdominal cramps. While similar manifestations of overdosage may be seen with mazindol, their exact nature have yet to be determined. The management of acute intoxication is largely symptomatic. Data are not available on the treatment of acute intoxication with mazindol by hemodialysis or peritoneal dialysis, but the substance is poorly soluble except at very acid pH.

How Supplied: Tablets, 1 mg. and 2 mg. in packages of 100.

Before prescribing or administering, see package circular for prescribing information.

SANOREX[®] (MAZINDOL) TABLETS, 1 mg. and 2 mg. in packages of 100.

CONSISTENT WEIGHT LOSS ON THE WAY TO THE TARGET WEIGHT



As a short-term adjunct in weight loss...

SANOREX[®] (MAZINDOL) TABLETS, 1 mg and 2 mg

For Brief Summary, please see facing page.

84N 8-074

Maybe I Wasn't So Wrong After All

On Population Control, Limits of Growth And the Side Effects of Sterilization

THE OTHER DAY I commented on a remarkable historic fact. "In our generation, the cult of fertility which dominated man's life as a factor of survival since paleolithic times has literally been stood on its head with the evolution of an anti-fertility cult of zero population growth (ZPG)." The subject is one constantly forced to my attention by an unceasing flood of correspondence, much of which is the most heated and most vituperative I've ever received.

Try as I do to keep the considerations of the issues calm, collected and in perspective, I just don't seem to be able to. Some years ago I had devoted considerable amount of time to the subject of population control. I have shared some of my observations with you and also presented them in a formal paper at the Colloquium of the International Association for Social Psychiatry in Honolulu.

Who Is Starving Now?

In essence, you may recall my belief that rate of population growth is primarily a socio-economic problem and not one of medical technology. I've found birth rates high when infant mortality is high and low when infant mortality is low and GNP (gross national product) high. My "calling" the facts as I saw them has been described by some as a lack of "concern" on my part. When I say I'm disturbed by our failure to feed those who were hungry and starving now, I'm accused of lack of sensitivity for those who may starve in the year 2,000.

Of course, I am not a demographer. I've approached available data with the humility of an ordinary physician fascinated by history, archaeology and research. I couldn't buy the ZPG concept as the only way out. I find neo-Malthusian doctrines scientifically distasteful, if not misleading. I have more faith in the imagination and ingenuity of man, perhaps even more than in man's judgments. In this regard, I was concerned about the Indian government's approach to its population prob-

lem many years ago and more recently outraged by its new initiatives. Perhaps I was not so far off. I now note newspaper stories on the failure of contraceptive technology in India, current reports of some leading demographers, and the fascinating shift in course of the prestigious, and highly visible and vocal Club of Rome. Let some news items tell the story:

For most other developing nations, demographers now admit they were unduly optimistic that modern medical technology could rapidly reduce birth rates... there's little evidence of success in nations with massive population reservoirs, particularly India, Pakistan and Bangladesh. "In the past... people felt with the technological breakthrough (in contraceptive methods) they would control world fertility in a decade; now there is a period of reassessment," notes Shigeni Kono, a United Nations demographer.

There's no doubt that birth control slows population growth. But its impact has been felt mainly in the developed nations. Many experts argue that modern contraception can accelerate a birth-rate decline that's already under way, but won't actually start a downturn.

So population planners are increasingly abandoning their emphasis on medical solutions to world population growth and focusing on longer-range remedies in social and economic development. Demographers note that birth rates tend to fall when income increases and is more evenly distributed when education is more widespread, and when more women participate in

Is tea harmful to your health? ...Well, maybe.

Medical Tribune Report

ANAHEIM, CALIF.—Two University of Hawaii nutritionists told the 60th annual meeting of the Federation of American Societies for Experimental Biology that 12 volunteers who laced otherwise nutritious diets with about a quart of tea a day came down with what looked like a "marginal to severe biochemical vitamin B₁ deficiency."

At the same time, tests for the blood enzyme transketolase and urinary thiamine indicated that the systems of the volunteers just

weren't absorbing the vitamin as well as they should. B₁, a participant in alpha-keto acid metabolism, is important in carbohydrate metabolism. Perhaps the tannin or caffeine in tea is responsible for blocking uptake of the vitamin, proposed Sandi Buhr and Dr. Doris Hiker.

Their research was the outgrowth of earlier work in Thailand which turned up a similar vitamin B₁ deficiency (fatigue, nervousness and loss of appetite) in residents of Thailand who subsisted mainly on betel nuts, fish and tea.

Medicine on Stamps

Jose Felipe Flores



Born in Chile, Jose Felipe Flores (1751-1824) received his medical degree from the University of Santiago in 1773. He joined the San Juan de Dios in Guatemala in 1785 as house surgeon. Later he studied anatomic dissection and preparation for surgery at European Universities. Upon his return to Guatemala, he constructed anatomic wax models that could be taken apart for teaching purposes.

Text: Dr. Joseph Klar
Stamp: Minkus Publications, Inc., New York

the work force. So said the *Wall Street Journal* of April 12, 1976.

Just one day later, the *New York Times* reported on the new position of the Club of Rome: The Club of Rome, which aroused intense controversy three years ago by the report it commissioned on "The Limits to Growth," now recognizes that further global growth is essential if the problems of world poverty and threats to world peace are to be solved.

The founder of the Club stated that the limits-to-growth report had served its purpose of "getting the world's attention" focused on the ecological dangers of unplanned and uncontrolled pollution and industrial expansion... The original study, based on a computerized model developed at the Massachusetts Institute of Technology, warned of a disaster to humankind within a century if present growth trends continued.

Vice-President Rockefeller, in a speech... attacked "no growth" economic and social philosophy, saying "It has always retarded some of the traditional dynamic thrust of the nation."

Further on one central aspect of the subject, I have had a recent exchange with some officials of the Association for Voluntary Sterilization. Because of their statement that vasectomy "has one of the lowest incidences of side effects when compared with other contraceptive methods," I pointed out that in their own literature the papers they were listing referred to the following side effects of vasectomy: hematoma, epididymitis, infection, sperm granuloma, sperm antibodies, thrombophlebitis, pulmonary embolism. These, of course, were in man; the side effects I had reported in our paper published in *Science* (179:293-5, Jan. 19, 1973) were in rats.

A new and lethal side effect of sterilization was reported in the *Washington Post* just a bit more than a week after the above two items:

Rioting left at least 10 dead in New Delhi when officials bulldozed houses of squatters offered to relocate them only if they would be sterilized.

Current Opinion

"Marijuana: A Return to Science"

J. THOMAS UNGERLEIDER, M.D.

Associate Professor of Psychiatry, UCLA Medical Center (Los Angeles, Cal.)
 Presidential Appointee, National Commission on Marijuana and Drug Abuse
 Director, UCLA Drug Abuse Training Center
 Director, UCLA Triage Multimodality Treatment Program
 Founder and Director, Project D.A.R.E. (Drug Abuse Research and Education)

SEVERAL YEARS AGO, the White House "declared war" on drug abuse. Subsequently, the phrase, "We have now turned the corner on drug abuse," was voiced every few months throughout the land. Yet, the drug problem remains. To continue to "turn the corner" is really to go around in a circle. However, perhaps we have turned the corner on some of our attitudes about the drug marijuana. It is a drug that has been used for centuries throughout the world.

In this country some 32 million persons have experimented with marijuana and over 13 million people continue to use it, at the last count. These figures contrast with the 100 million regular users of alcohol in our country.

The allegations and mythology about marijuana which first began here in the mid-1930's bear scrutiny. It was once said that the derivative of the word "hashish" from "assassin" had to do with its violence-producing properties. Students of mythology however, quickly pointed out that the hashish was used as a reward for, and thus conditioning to, acts of violence committed while not intoxicated. Today, in fact, the various militant groups strongly prohibit use of drugs like marijuana by their members because such drug use distracts them, in a non-goal directed and peaceful fashion, from their purpose of disruption, change, and/or revolution.

"Amotivational Syndrome"

As the violence theory fell from favor, concern about the opposite effects was advanced. This involved the so-called "amotivational syndrome" or loss of incentive resulting from marijuana use. Concern was expressed that many young people, in particular, would lead less productive lives because of the sedative effects from regular marijuana use. However, longitudinal studies of thousands of college students plus studies of post-graduate students (medical and law students) have revealed no significant difference in grades between users and non-users. The government studies of heavy long-term users in Jamaica, Costa Rica, and Greece have also failed to substantiate the existence of such a syndrome.

The Domino Theory

Next, the stepping-stone or domino theory was advanced. This theory claimed that use of marijuana led ultimately to heroin use. Indeed, some 85% of heroin "addicts" have used marijuana. Although no one knows how many heroin addicts there are in this country, despite the alleged state of "epidemic" (official estimates to our National Commission on Marijuana and Drug Abuse ranged from 200,000 to 750,000 active addicts), virtually every study has shown that alcohol and nicotine are the initial drugs of experimentation by our heroin addicts (95% have used alcohol) and everyone else as well. If one has not used alcohol or cigarettes, one rarely uses other kinds of psychotropic drugs of any kind.

LSD, but some had epilepsy and others a history of cerebral trauma. The brain damage theory too has never been substantiated. None of the alleged "chronic brain syndrome" patients from hashish use in Morocco, Greece, Afghanistan, India, or Egypt have ever been produced.

Marijuana was next alleged to affect the body's immune mechanisms in vitro. These findings have never been replicated, although they received wide publicity. Similarly, initial case reports of genetic and chromosome changes in rats have remained unconfirmed areas of concern about the human consumption of marijuana.

New Clarifying Studies

And, once again, we see the opposite. Now the (often double-blind) reports of the medical usefulness of marijuana

(a drug used for centuries in folk medicine throughout the world) are being issued. The use of cannabis in glaucoma and asthma and to reduce nausea and vomiting in cancer patients receiving chemotherapy has recently received much publicity, as a number of medical reports have appeared in the literature.

Fear of sexual license and the aphrodisiac qualities of marijuana resulted from varied and scattered anecdotal reports which were never confirmed from the experimentation conducted subsequent to the synthesis of THC (tetrahydrocannabinol), the active ingredient of marijuana, in 1966. The opposite fears were then expressed, those of impotence or lack of performance. This was inferred from one (unsubstantiated) report of gynecomasia and several reports of temporarily lowered testosterone levels after use

of marijuana. Currently, experimentally, doses of the THC hundreds of times larger than those normally given by smokers are currently being given to human subjects. The fact that these subjects live (and have minimal discomfort), where with comparable doses of many other experimental drugs they would die, only attests to the widespread margin of safety with marijuana.

Moving to social policy, medicine, and marijuana, a recent argument against decriminalization is that marijuana is fat soluble, like DDT, and remains for approximately eight days in the body. How fatty tissue content relates to jail sentences remains reconcilable, however. Some cite intent as an important factor. They claim that alcohol is consumed to socialize but not to get "high," and that alcohol intoxica-

tion is but an unfortunate result (with its 35,000 traffic fatalities, 1 million traffic accidents, and one half of all violent crimes associated with alcohol each year in our country alone). Marijuana, by this reasoning, is taken solely for the pleasure that results from the "high" state. Thus, socializing (vis-à-vis alcohol) becomes desirable and getting "high" (from marijuana) undesirable—an exercise in semantics.

Students of behavior and the curious onlooker should find these arguments and the debate fascinating, for the real issue may well lie elsewhere—with morality and pleasure. Is one psychotropic drug "good" and another "bad" or are both merely chemicals with effects and side-effects? Should taking a particular chemical in private for pleasure, when not medically prescribed, be penalized by the criminal justice sys-

tem or should health problems that result be handled by the health care professionals and should proscribed behavior be limited to that which directly influences others (i.e., driving under the influence—there are now tests for marijuana in the body fluids)? Further, what about using a drug for other than its intended use (i.e., amphetamines for a morning "lift," not for obesity control) or those who self-medicate in general—should these people be subjected to criminal sanctions for their "misuse" of drugs?

Our Role as Physicians

This past year, seven additional states (Alaska, Maine, Colorado, California, Ohio, South Dakota, and Minnesota) have joined Oregon in forms of decriminalization of the personal use of marijuana. Bills are pending in over

a dozen more states and federally, in both houses of Congress. Thus, major changes are occurring regarding our attitudes and subsequent social policy regarding criminalization of the casual marijuana user.

For us as physicians and scientists, professional input seemingly should be limited to determining if marijuana is a threat to the public health, safety, or welfare of our nation. If so, we should consider retention of strong negative sanctions and enforce them equally via the criminal justice system. However, the evidence is overwhelming that marijuana is not such a threat. Even in those cultures where marijuana has been used for many decades and hundreds of years in heavy doses, it is no major threat to the public health, safety, or welfare. This spring, the annual HEW report to Congress on "Marijuana and Health" finally officially stated such a position for the United States.

So, finally, for marijuana, the issue has now become less controversial; medicine seems to be returning to science, politicians to truth, and the public to sanity.

Glycol Solvent Used in Phenol Burn Therapy

Medical Tribune Report

SAN ANTONIO—The use of pure water should be avoided in the emergency treatment of severe phenol burns, according to Dr. Russel Pardoe, chief of the Division of Plastic and Reconstructive Surgery at Santa Clara Valley Medical Center in San Jose, Calif.

The best solvent to use is polyethylene glycol 400, diluted 50% with water, Dr. Pardoe told the American Burn Association meeting here. Undiluted polyethylene glycol absorbs water, has a hentive dilution of about 10°C, and would introduce the risk of further thermal injury. Diluted, however, the polyethylene is "less viscous," and it "is an extremely good solvent for the phenol. It will take out other chemicals that might have been mixed with the phenol, and it doesn't have toxic fumes," Dr. Pardoe said.

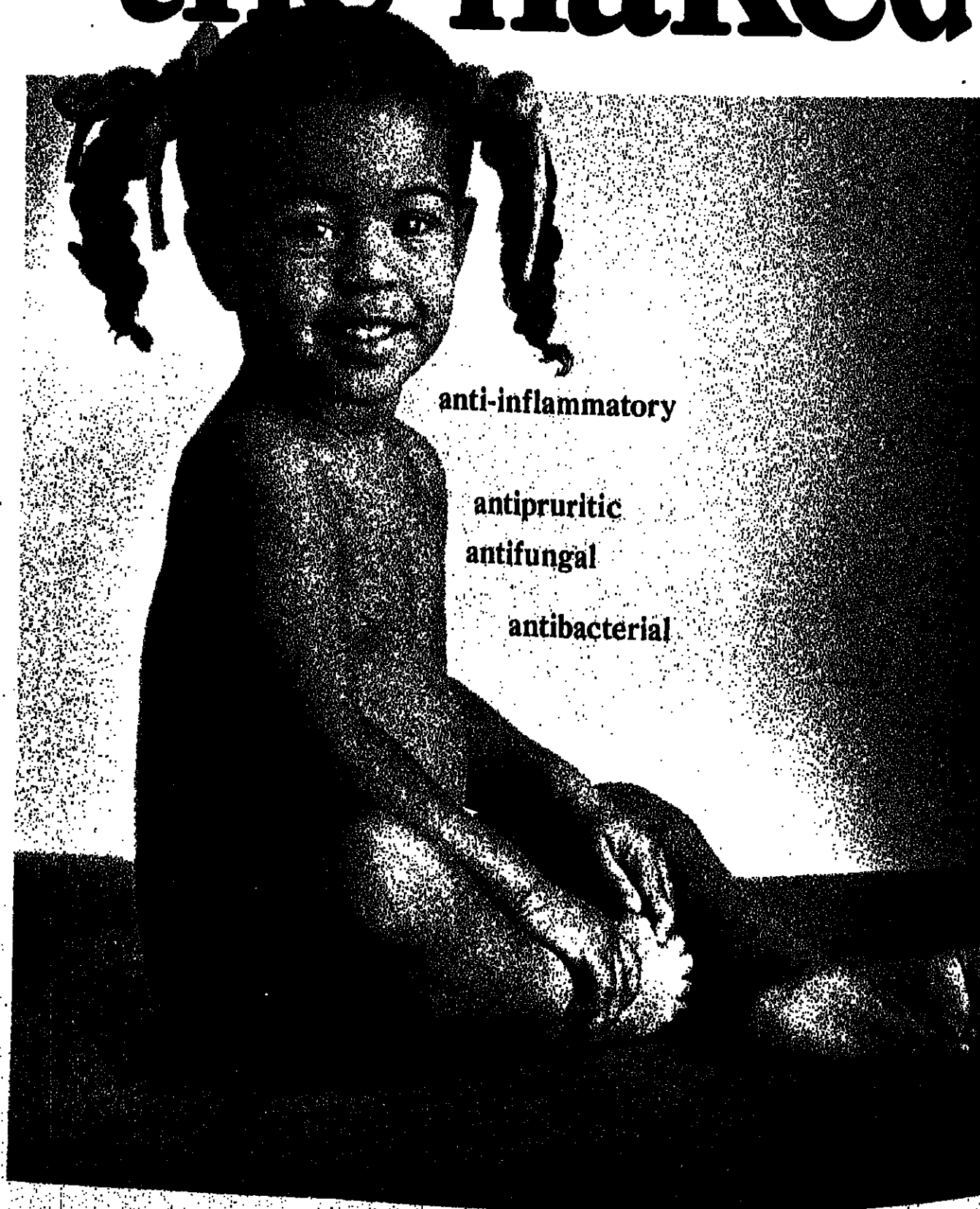
Phenol is now being used more commonly than before in household products such as dry cleaning fluids, Dr. Pardoe said. One man that he treated had left cleaning fluid on his trousers for 24 hours, and it burned through the skin to his kneecap.

Dr. Pardoe stressed however, that the best and cheapest form of treatment for any burns is prevention. He said any factory or establishment that has phenol on the premises should be very well prepared.

"It's important to have rescue gear and first aid equipment and good communications," he said.

Protective clothing of proper design is important not only for employees working in areas where phenol is stored or used, but also for the rescue team as well. Dr. Pardoe cited one industrial accident in which about 15 rescuers sustained burns. The only man who was wearing protective clothing in that accident received the deepest burn because his clothing trapped the phenol solution around his belt and in his boots.

the naked truth...



anti-inflammatory

antipruritic

antifungal

antibacterial

Today a child's skin problem is harder to hide, but easier to treat...with Vioform-Hydrocortisone.

The four-way action of Vioform-Hydrocortisone provides the kind of comprehensive therapy that many common dermatoses* may require, particularly those infected with bacteria or fungi.

*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

Vioform-Hydrocortisone
 (iodochlorhydroxyquin and hydrocortisone)

INDICATIONS
 Based on a review of this drug by the National Academy of Sciences-National Research Council and for other information, FDA has classified the indications as follows:
 "Possibly" effective: Contact or atopic dermatitis; impetigo; eczema; nummular eczema; infantile eczema; atopic chronic infectious dermatitis; stasis dermatitis; psoriasis; nuchal eczema and chronic eczematoid otitis externa; some localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (pruritus, scroti, an); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis) moniliales; Intertrigo.
 Full classification of the less-than-effective indications require further investigation.

CONTRAINDICATIONS
 Sensitivity to Vioform-Hydrocortisone, or any of its ingredients; viral or bacterial lesions of the eye; tuberculous of the skin; viral skin lesions (including herpes simplex, varicella, and chickenpox).
WARNINGS
 This product is not for ophthalmic use.
 In the presence of systemic infections, appropriate systemic anti-infectives should be used.
 Use in Pregnancy
 Although topical steroids have not been reported to have systemic effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant women in large amounts or for prolonged periods of time.

Vioform-Hydrocortisone
 (iodochlorhydroxyquin and hydrocortisone)

the most widely
 prescribed form...
 20 Gm Cream

C I B A

Vicki Morison Administration Manager
 Isabel Hutchings Conference Manager
 Charlotte Benton-Hughes Conference Ass.
 Kerry Brown Technical Services Manager

Tel: 081 332 2422
 Fax: 081 332 0939

Tribune Economic Analysis



High Interest by Mexican Banks Equals High Risk

BY ELIOT JANEWAY
Consulting Economist

The buildup for Mexico's devaluation of the peso started last winter. A major public relations campaign was launched to dramatize Mexico's presence in the line-up of oil exporting countries. The idea was that Mexico could be trusted to clean up along with the members of the oil cartel at the expense of the oil "have nots." She used the oil sales buildup as a come-on to creditors large and small.

Under cover of this barrage of bravado about her coming oil prosperity, Mexico managed to borrow something like £600 million in the London Euromarket. When she did so, the British pound was still closer to \$2.20 than to its present low level of \$1.82. This meant that she could do more with the British money she took abroad than anyone else.

Moreover, it seems that Mexico is now admitting to a trade deficit of \$3.6 billion. Her oil trade netted her an off-setting surplus of only \$112 million—peanuts!

The lure of high interest rates has attracted hard U.S. dollars into Mexico. The record of stability for the peso and reliability of Mexican banks of deposit, as well as bonds, has reassured American savers and investors who started out being wary.

Doctors and Dentists

Guessimates vary, but the \$4 billion showing up as U.S. retail deposits is low. Allowing for all the tax evasion money that regularly slips across the border, even \$6 billion seems like a low figure. Mexico has been an irresistible haven for the kind of money that's intent on beating the game—especially that of doctors and dentists with notoriously poor speculative records. My repeated warnings that the double-digit interest rates Mexico offers foreign depositors are a more faithful measure of risk than reward have stirred up more than my normal quota of disbelief and controversy.

The British have a phrase for the kind of expatriate money that has been trying to enjoy the best of all worlds in Mexico: "tooclever by half." No one can fairly fault the American banks for this. They are owed too much money for comfort by borrowers in the devaluation belt.

Ask Janeway

Some of the weaker alibis seem to have weathered the financial storm with their convertible debentures selling at two-digit yields. What would you think of them?

M.D. Bond-buyer

Smart idea.

Send your questions on finances, investments, taxes to Janeway, MEDICAL TRIBUNE, 880 Third Avenue, New York, N.Y. 10022.

One of the most important things about this drug is who not to prescribe it for.

The wrong drug for these patients

Patients with impaired renal function or hepatic disease.

Patients who have a history of lactic acidosis or who drink alcohol in excess.

Patients with acute complications of diabetes mellitus, or during or immediately following surgery, where insulin is indispensable.

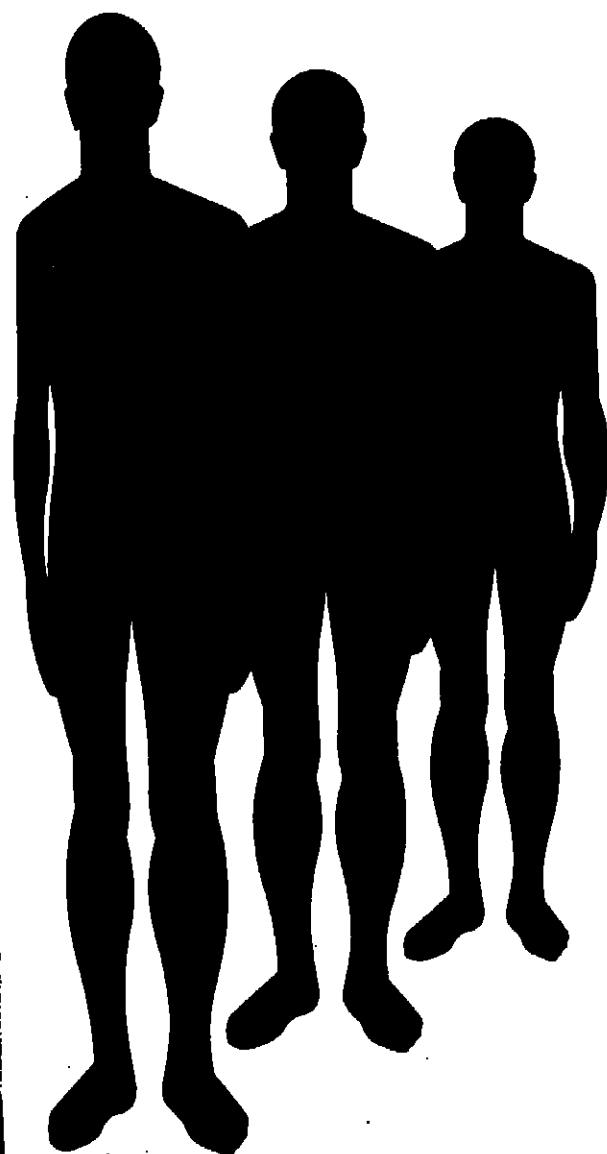
Patients with cardiovascular collapse (shock), congestive heart failure, and after disease states associated with hypoxemia.

The right drug for the right patient

DBI-TD phenformin HCl may be the right drug for the otherwise healthy, overweight, adult-onset, nonketotic diabetic who cannot be controlled by diet alone, and who does not have increased risk of lactic acidosis.

When to stop the drug

Patients should be instructed to discontinue medication and notify their physicians immediately if G.I. symptoms, hyperventilation or other acute illness should occur.



DBI-TD[®] phenformin HCl

May be the right drug for the right patient because it lowers blood sugar without raising blood insulin, and excess insulin often leads to weight gain.

For full details, please read the prescribing information summarized below.

Geigy

DBI[®] phenformin HCl USP Tablets of 25 mg.

DBI-TD[®] phenformin HCl Timed-Disintegration Capsules of 50 mg.

WARNING: THERE HAVE BEEN NUMEROUS REPORTS OF LACTIC ACIDOSIS IN PATIENTS RECEIVING PHENFORMIN. LACTIC ACIDOSIS IS AN OFTEN FATAL METABOLIC ACIDOSIS. READ THE WARNINGS SECTION CAREFULLY BEFORE PRESCRIBING THIS DRUG.

Indications: Stable, adult diabetes mellitus; autolytic failures; primary and secondary. **Contraindications:** Diabetes mellitus that can be regulated by diet alone; hypersensitivity to phenformin; renal disease with impaired renal function; a history of lactic acidosis; alcoholism; juvenile diabetes mellitus that is uncomplicated

and well regulated on insulin; acute complications of diabetes mellitus (metabolic acidosis, coma, infection, gangrene); during or immediately after surgery where insulin is indispensable; acute or chronic liver disease; cardiovascular collapse (shock); after disease states associated with hypoxemia. **Warnings:** Patients should be warned to discontinue phenformin and notify the treating physician promptly if clinical illness develops, especially vague and poorly defined illness. **Lactic Acidosis:** This is characterized by elevated lactate levels, an increased lactate-to-pyruvate ratio, and decreased blood pH. In most cases, azotemia ranging from mild to severe was present. This may have been the result of dehydration. In some patients who developed lactic acidosis, serum creatinine was later within normal limits when the patients were properly hydrated. Observe the following specific warnings: a. Impairment of renal function increases the risk of lactic acidosis. Perform renal function tests,

such as serum creatinine, prior to phenformin therapy and at least every six months thereafter. Phenformin is contraindicated in patients with even mild degrees of impaired renal function. b. Cardiovascular collapse (shock), congestive heart failure, acute myocardial infarction, and other conditions characterized by hypoxemia also may cause prerenal azotemia and have been associated with lactic acidosis and other conditions characterized by hypoxemia. c. Gastrointestinal disturbances are the most common adverse reactions of phenformin therapy and must be distinguished from the prodromal signs of lactic acidosis. Anorexia and mild nausea are not uncommon side effects, particularly upon initiation of therapy. Nausea, vomiting, hyperventilation, malaise, or abdominal pain may herald the onset of lactic acidosis. Instruct the patient to discontinue phenformin and notify the physician immediately

should any of these symptoms occur. Withdraw phenformin until the situation is clarified by determination of electrolytes, pH, blood sugar, ketones, lactate, and pyruvate. d. Lactic acidosis has a significant mortality. When suspected, discontinue phenformin and institute intravenous infusions and other appropriate therapy, even before the results of lactate determinations are available. It should be suspected in the presence of a metabolic acidosis in any diabetic patient lacking evidence of ketoacidosis (ketonuria and ketonemia) and not intoxicated with methanol or salicylates, or not in sinus acidosis. e. Use special caution after initiation of phenformin therapy, after increase of drug dosage, and in circumstances that may cause dehydration leading to impaired renal function. f. Warn patients against using alcohol in excess while receiving phenformin, since ethanol and phenformin potentiate the tendency of each to cause an elevation of blood lactate levels.

Pregnancy: Use during pregnancy is to be avoided.

Precautions: Starvation Ketosis: This must be differentiated from "insulin lack" ketosis and is characterized by ketonuria, in spite of relatively normal blood sugar with little or no urinary sugar. This may result from excessive phenformin therapy or insufficient carbohydrate intake. "Destabilization" of Previously Controlled Diabetic: When laboratory abnormalities or clinical illness develop, evaluate electrolytes, pH, lactate, pyruvate, and blood and urine ketones for evidence of ketoacidosis or lactic acidosis. With either form, withdraw phenformin and institute corrective therapy. **Hypoglycemia:** Although hypoglycemic reactions are rare when phenformin is used alone, every precaution should be observed during the dosage adjustment period particularly when a sulfonylurea has been given in combination with phenformin. **Adverse Reactions:** Principally gastrointestinal;

unpleasant metallic taste, continuing to anorexia, nausea and, less frequently, vomiting and diarrhea. Reduce dosage at first sign of these symptoms. In case of vomiting, the drug should be immediately withdrawn. Although rare, urticaria has been reported, as have gastrointestinal symptoms such as anorexia, nausea and vomiting following excessive alcohol intake. There have been isolated reports of macrocytic anemia, and evidence of impaired vitamin B₁₂ absorption in patients treated with phenformin. (B) 98-148-103-J (Rev. 5/78) 687 181 C78-6 For complete details, including administration and dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

028 11722

Questions Raised On Worth, Safety Of Infant Dieting

Continued from page 1

University of Rochester School of Medicine, was designed to test the hypothesis that "there is a significant correlation between weight gained in the first six months of life and adult weight status in the third decade of life," Dr. Charney, now Associate Professor of Pediatrics at Johns Hopkins School of Medicine and Professor of Pediatrics at the University of Maryland School of Medicine, said.

His research team also examined the effects of birth weight, rate of weight gain, height, sex, the order of birth in the sibling line, breast feeding, social and educational status, and current weight of the parents. Only the last two factors influenced adult weight, Dr. Charney said, and neither was as influential as weight at six months, the earliest known correlate to both adult overweight and underweight.

Study Population

The study sample included 366 patients, divided into three groups based on their medical records: heavy infants (weight exceeded 90th percentile at least once), average infants (weight ranged between 25th and 75th percentiles) and lightweight infants (weight was below 10th percentile at least once).

All patients currently more than 10% above the medium weight for their height and age were defined as overweight, Dr. Charney said. If more than 20% over, they were classed as obese. The scale used was the 1962 National Health Survey for normative height and weight, which gave heavier weights than previously reported. A total of 406 subjects, now between 20 and 30 years, were sent questionnaires, with a 94% compliance rate. The sample was "not necessarily a representative one of children cared for in the pediatric practices [of three coauthors, Drs. Burtis Breese, Frank Disney, and Kurt Marx], but has been stratified to select approximately equal cohorts of heavy, average, and lightweight infants," Dr. Charney explained.

To check the veracity of subjects' answers, Dr. Charney's group also invited 50 patients living in the Rochester area to come in for a personal interview. When their actual height and weight were compared to their answers on the questionnaire, Dr. Charney found that "37 of the 50 weighed more than they thought, and 31 were an inch shorter than they hoped." Several subjects, he said, were skeptical of his scales and demanded a second weigh-in. A 5% correction factor was promptly applied to the questionnaire data.

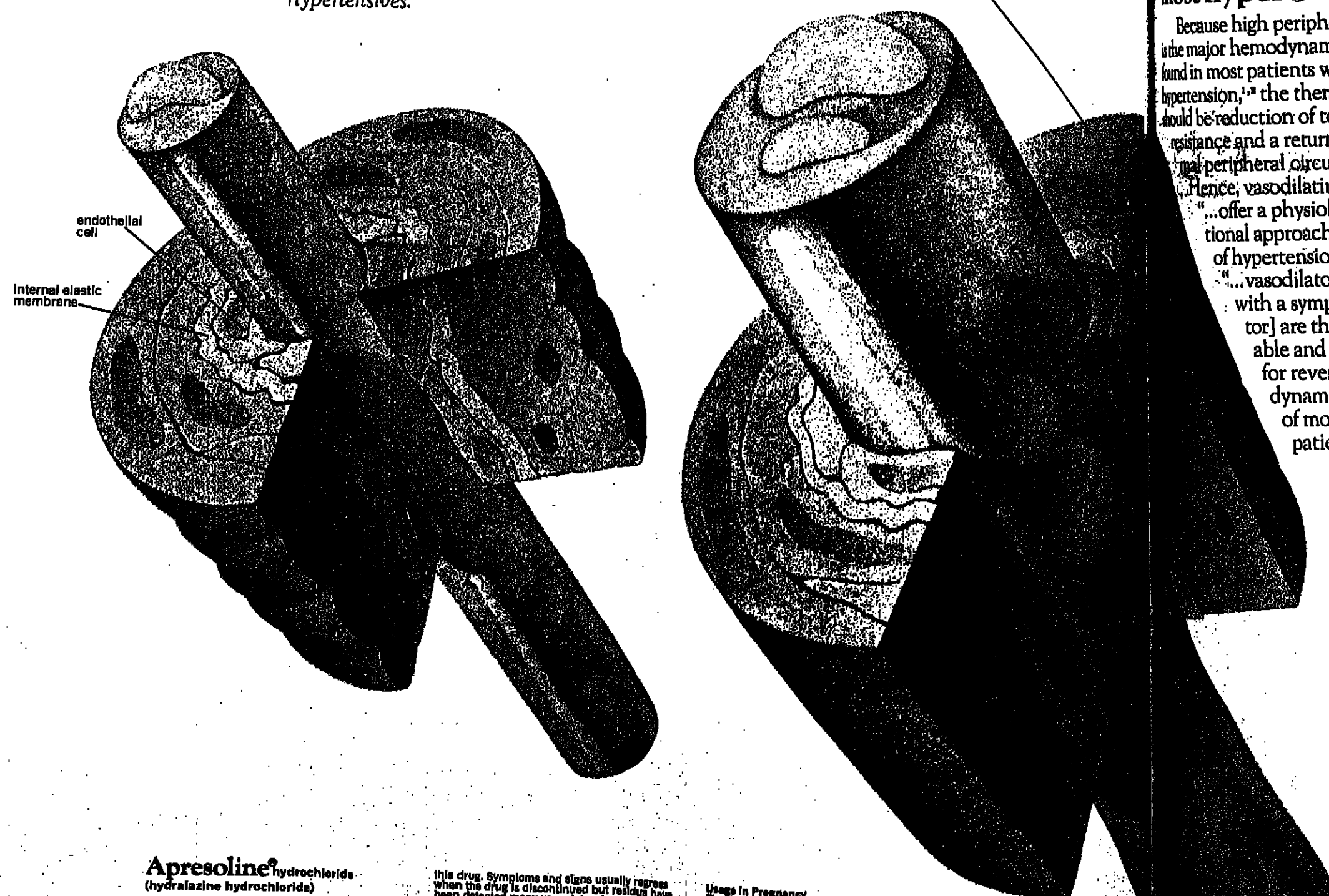
"Thirty-six percent of the infants exceeding the 90th percentile were overweight or obese adults," Dr. Charney found, "compared to 14% of both other groups ($p < .001$). We can also look at the correlation between the child's maximum weight percentile in the first six months and his adult status."

Continued on page 27

Apresoline... (hydralazine) relaxes arterioles to solve the major hemodynamic problem in hypertension

Abnormally high peripheral resistance is the major hemodynamic problem with most hypertensives.

Apresoline reduces peripheral resistance and lowers blood pressure through a direct relaxation of arteriolar smooth muscle.



high peripheral resistance: common attribute of most hypertensives

Because high peripheral resistance is the major hemodynamic disturbance found in most patients with essential hypertension,^{1,2} the therapeutic goal should be reduction of total peripheral resistance and a return to more normal peripheral circulation.

Hence, vasodilating drugs "...offer a physiologically rational approach to the therapy of hypertension."³ In addition, "...vasodilators [combined with a sympathetic inhibitor] are the most predictable and specific drugs for reversing the hemodynamic abnormality of most hypertensive patients."⁴

the only oral agent that deals directly with this problem

Apresoline (hydralazine) is the only currently approved oral antihypertensive with vasodilating action; decreases peripheral resistance—regardless of its cause—and, hence, arterial pressure by relaxing arteriolar smooth muscle. Accompanying the fall in blood pressure is a rise in cardiac output and rate. Apresoline also maintains or increases renal and cerebral blood flow.

a different and complementary pharmacologic approach

Different in action from all other oral antihypertensives and compatible with most of them, Apresoline can play a significant role in a variety of therapeutic combinations.

Such combinations, according to Freis,⁵ with each component representing a different antihypertensive mechanism,

provide the most effective way to control blood pressure. This approach may also permit lower drug dosages.

the problem of postural hypotension minimized

Nickerson⁶ describes the action of Apresoline as follows:
"A preferential effect on arterioles, as compared to veins, allows the increase in cardiac output and minimizes postural hypotension; the latter is much less than that produced by agents blocking sympathetic nerves."

Continued on following page

Apresoline® hydrochloride (hydralazine hydrochloride)

TABLETS

INDICATIONS

Essential hypertension, alone or as an adjunct.

CONTRAINDICATIONS

Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.

WARNINGS

Hydralazine may produce in a few patients a clinical picture simulating systemic lupus erythematosus. In such patients hydralazine should be discontinued unless the benefit to risk determination requires continued antihypertensive therapy with

this drug. Symptoms and signs usually regress when the drug is discontinued but residues have been detected many years later. Long-term treatment with steroids may be necessary.

Complete blood counts, L.E. cell preparations and antinuclear antibody determinations are indicated before and periodically during prolonged therapy even though patient is asymptomatic. These studies are also indicated in the presence of any unexplained symptoms.

A positive antinuclear antibody titer and/or positive L.E. cell reaction requires that the physician carefully weigh the implications of the test results against the benefit to be derived from antihypertensive therapy with hydralazine.

Use MAO inhibitors with caution.

Use in Pregnancy

The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

PRECAUTIONS

Use cautiously in suspected coronary artery or other cardiovascular diseases, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.

Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antihypertensive effect and addition of pyridoxine to the regimen if symptoms develop.

Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue

therapy. Periodic blood counts are advised during prolonged therapy.

ADVERSE REACTIONS

Common: Headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. Less frequent: nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremor; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia,

agranulocytosis, and purpura; hypotension; paradoxical pressor response.

DOSEAGE

Initiate therapy in gradually increasing dosages, adjust according to individual response. Start with 10 mg 4 times daily for the first 2 to 4 days, increase to 25 mg 4 times daily for balance of first week. For second and subsequent weeks, increase dosage to 50 mg 4 times daily. For maintenance, adjust dosage to lowest effective level. The incidence of toxic reactions, particularly the L.E. cell syndrome, is high in the group of patients receiving large doses of Apresoline. In a few resistant patients, up to 300 mg Apresoline daily may be required for a significant antihypertensive effect. In such cases, a lower dosage of Apresoline combined with a diuretic, reserpine, or

both may be considered. However, when combining therapy, individual titration is essential to insure the lowest possible therapeutic dose of each drug.

HOW SUPPLIED
Tablets, 10 mg (pale yellow, dry-coated); bottles of 30, 60, 100 and 1000.
Tablets, 25 mg (deep blue, dry-coated) and 50 mg (pale, dry-coated); bottles of 30, 60, 100, 500 and 1000.

Tablets, 100 mg (peach, dry-coated); bottles of 100.
Consult complete literature before prescribing.

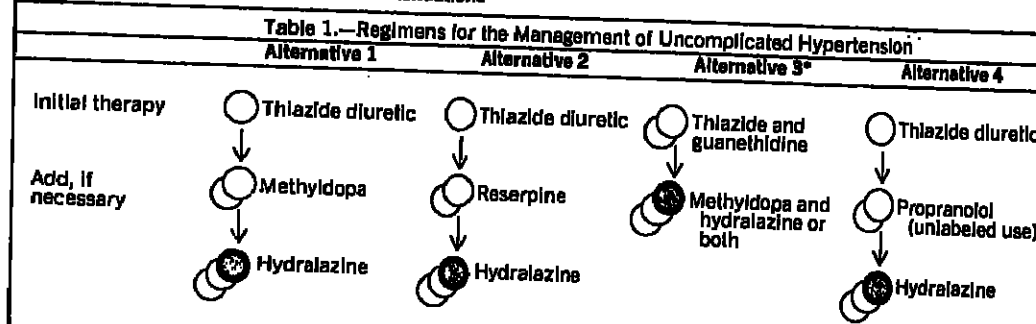
CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

C I B A

Apresoline® (hydralazine)

...key component in the "guideline" antihypertensive regimens

AMA Committee on Hypertension Recommendations

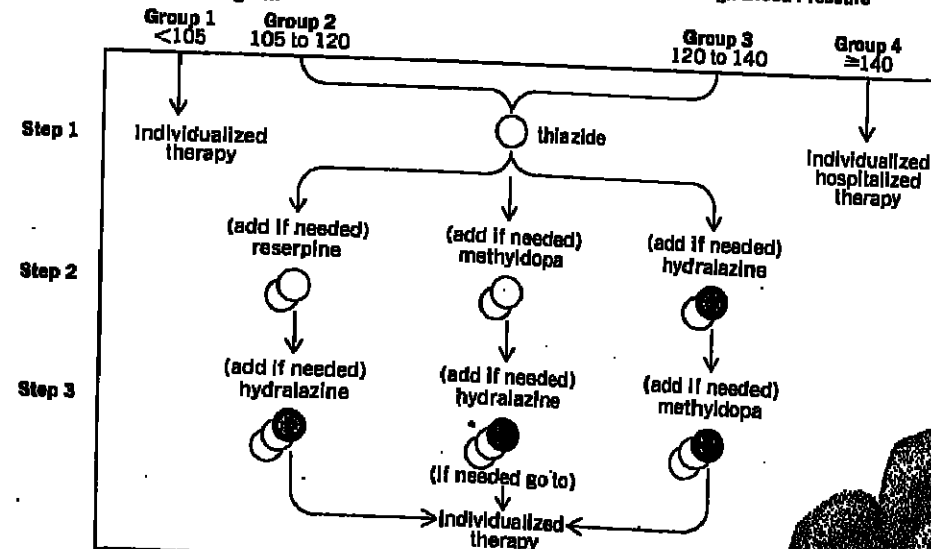


*In patients who cannot tolerate guanethidine, alternatives 1 or 4 may be given a therapeutic trial, but treatment should be initiated with both the diuretic and methyldopa or propranolol.

Apresoline...
included in all four
treatment plans by the
AMA Committee*

(Adapted*)

Recommendations by the Hypertension Task Force of the National High Blood Pressure Education Program



Therapeutic Objective: Diastolic pressure under 90 mm Hg, or, if untoward effects cannot be tolerated, under 100 mm Hg.

used effectively in the
landmark VA
studies^{8,9}

Apresoline was one of the three basic drugs used in two published VA cooperative studies—studies which demonstrated conclusively the benefits of antihypertensive treatment in reducing risk of morbidity and mortality.

Apresoline...
(hydralazine)
An antihypertensive
idea whose time
has come



Apresoline...
recommended second
and third step therapy
by the Hypertension
Task Force*

(Adapted*)

References
1. McNay JL. Adrenolytic and vasodilator therapy. *Postgrad Med* 56:76-80, 1974.
2. Koch-Weser J. Vasodilator drugs in the treatment of hypertension. *Arch Intern Med* 133:1017-1027, 1974.
3. Koch-Weser J. The vasodilator antihypertensives. *Drug Therapy* 5:67-81, 1975.
4. Fries ED. Hypertension: A controllable disease. *Clin Pharmacol Ther* 13:457-459, 1972.
5. Nickerson M. Antihypertensive agents and the drug therapy of hypertension. In Goodman LA, Gilman A (eds). *The Pharmacological Basis of Therapeutics*, ed 4. New York, The Macmillan Company, 1970, p 728.
6. Committee on Hypertension: Drug treatment of ambulatory patients with hypertension. *JAMA* 228:1647-1659, 1973.
7. Report of Task Force I, National High Blood Pressure Education Program: Recommendations for a National High Blood Pressure Program Data Base for Effective Antihypertensive Therapy, Sept 1, 1973. DHEW Publication No. (NIH) 74-593.
8. Effects of treatment on morbidity in hypertension. Results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 202:1028-1034, 1967.
9. Effects of treatment on morbidity in hypertension II. Results in patients with diastolic blood pressures averaging 90 through 114 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 213:1143-1152, 1975.

C I B A

Chubby Infants: Is Early Dieting Worthwhile?

Continued from page 23

"The risk appears stable below the 75th percentile (12.5% will be overweight at 18%, 33%, and 40%," he said. "Thus infants above the 90th percentile have a two-and-a-half times greater risk of later obesity, compared with other groups," he pointed out.

In the tall, heavy infant at less risk of adult obesity than the short heavy one? "Many clinicians have assumed that to be the case and so assured themselves and the parents," Dr. Charney noted. However, the study showed that absolute weight gained at six months was the critical variable, "quite independent of the infant's length."

The findings also confirmed the well-known fact that the higher the social class or educational level, the less chance the subject has of obesity, independent of other factors. In addition, the current weight status of the parents showed a striking relationship to obesity in the child," Dr. Charney reported. "When at least one parent is overweight and the infant's weight is above the 75th percentile, then 51% are overweight or obese as adults."

In the group as a whole, "two-thirds of all the overweight and obese adults were identifiable by six months of age," Dr. Charney concluded.

from Germany Food Allergen Cut Ameliorates Acne

Continued from page 17

Food, patients were instructed to avoid positive allergens so detected for a

few weeks; patients reacting positively to the cheese test were additionally recommended to give up yogurt and curds, and to reduce their consumption of veal and beef. Correlation between the ingestion of positive allergens and renewed onset of the skin condition was so evident that the patients in general willingly forwent the prohibited foods although these had been quite frequently their favorite dishes. Continuance of the elimination diet over a fairly long period was obtainable for the most part only with patients who could take care of themselves at home; relapses frequently occurred with those feeding in canteens and restaurants,

where particular condiments could not be pinpointed.

The diet was classed therapeutically successful (very good to good) in 281 patients who could be discharged practically free from acne at the end of the course. A clear improvement was obtained in a further 96 patients, although strict adherence to the diet could not be verified over a longer period. Only 23 patients, mostly very young, who did not adhere to the elimination diet, presented no improvement.

View Supported

These results support Dr. Obeldi-Ruggli's view that the development of

In cerebral and peripheral ischemia associated with arterial spasm



In cerebral ischemia:

direct vasodilation of cerebral vessels; virtually no CNS effect; rare incidence of side effects permits long-term use

In peripheral vascular disorders:
relaxes smooth muscles of larger blood vessels by direct effect unrelated to muscle innervation

For additional product information and professional samples, write on your letterhead to
Professional Service Department
KENWOOD LABORATORIES, INC.
New Rochelle, New York 10801

Indications: For the relief of cerebral and peripheral ischemia associated with arterial spasm.

Contraindications: The use of ethaverine hydrochloride is contraindicated in the presence of complete atrioventricular dissociation.

Precautions: Use with caution in patients with glaucoma. Hepatic hypersensitivity has been reported with gastrointestinal symptoms, jaundice, eosinophilia and altered liver function tests. Discontinue drug if these occur.

The safety of ethaverine hydrochloride during pregnancy or lactation has not been established; therefore it should not be used in pregnant women or in women of childbearing age unless, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

Adverse Reactions: Although occurring rarely, the reported side effects of ethaverine include nausea, abdominal distress, hypotension, anorexia, constipation or diarrhea, skin rash, malaise, drowsiness, vertigo, sweating, and headache.

Dosage and Administration: One capsule three times a day.

How Supplied: 100 mg capsules in bottles of 50 and 500.

from France

Use Arteriography In Insufficiency Dx

Continued from page 17

order of consciousness or vegetative systems).

Angiographic assessment is difficult because of the length of time required, the amount of iodized product injected and the frailty of the patient. Vasodilators, administered in strong doses by perfusion, are required before and after the angiography, which should always be performed during a three-to-four day hospitalization. General anesthesia must be given carefully, with supervision focusing particularly on functional variations.

Indications for Surgery

Medical treatment of cerebral circulatory insufficiency, said Professor Jomin, is essentially based on the vasodilators, the results of which are debatable, on medications with a metabolic cerebral action, and on platelet anti-aggregators. Surgical treatment consists of endarterectomy alone or combined with restorative surgery. It is a simple, mild and rapid operation, yielding good results in 88% of the patients. Operative mortality is below 2%. Surgery is indisputably indicated in case of recurring incidents. However, surgery is contraindicated when dealing with an acute and/or definitive neurologic accident.

ILX B12

hematinics
of
choice

By teaspoon or tablet
• Readily assimilated
• Well tolerated
• Economical

for
nutritional
and iron
deficiency
anemias

Usual Dosage: ELIXIR—1 to 3 teaspoons daily or as directed by physician.
TABLETS—1 tablet 3 times a day or as directed by physician.
Supplied: 12 ounce bottles of Elixir; bottles of 100 Tablets.

K Kenwood Laboratories, Inc., New Rochelle, New York 10801
Developers and suppliers of Cerebral and Kengear

ILX B12TM
Elixir—each ounce represents: Iron and Ammonium Citrate, 18 gr • Liver Fraction 1:3 gr • Thiamine Hydrochloride, 10 mg • Riboflavin, 4 mg • Nicotinamide, 20 mg • Cyanocobalamin (Vit. B12), 20 mcg • Alcohol 8% by volume.
Tablets—each tablet contains: Ferrous Gluconate, 5 gr • Vitamin C, 60 mg • Cyanocobalamin (Vit. B12), 10 mcg • Liver Fraction 2:2 gr • Thiamine Hydrochloride, 2 mg • Riboflavin, 2 mg • Nicotinamide, 20 mg

on average, sleep
within 17 minutes that
lasts for 7 to 8 hours
with fewer nighttime
awakenings¹ proved in patients
with insomnia in 8 sleep research laboratory
studies

for patients who need it, continued
effectiveness over 28 nights^{2,3}

prolonged medication for insomnia is generally not necessary;
should it be, the only available sleep agent proved objectively to be
effective longer than two weeks is Dalmane (flurazepam HCl)

proven effectiveness in
elderly patients with
verified insomnia⁴

the greater the degree of insomnia, the greater
the objective improvement with Dalmane 15 mg
administered for 7 nights h.s.—15 mg is the
recommended initial dosage for elderly and
debilitated to help preclude oversedation,
dizziness or ataxia

a full night's sleep with a single
h.s. dose¹⁻⁸ patients fall asleep faster, awaken less often
during the night, sleep longer without repeating dosage

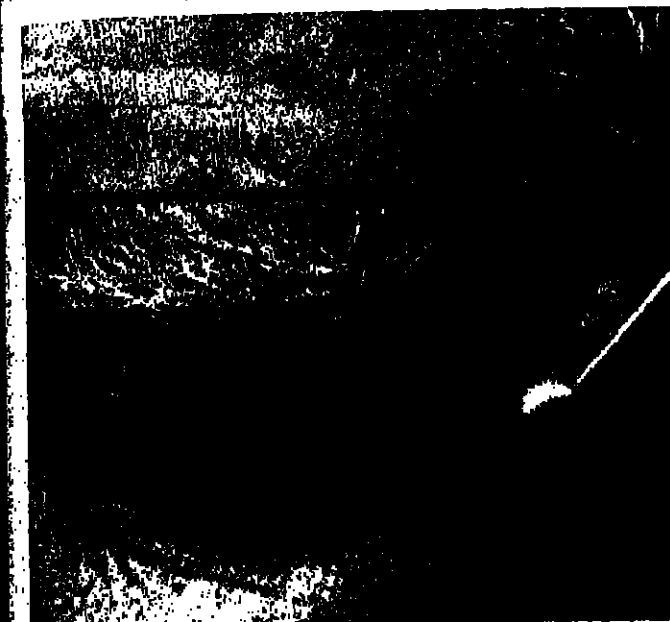
well tolerated, seldom
causes morning
"hang-over"¹ Dalmane is a

distinctive benzodiazepine specifically indicated for
sleep with well-documented safety and low
incidence of morning "hang-over"

more documentation from the
sleep research laboratory than
any other agent for insomnia¹⁻⁸

polysomnographic techniques provide the most objective
measurement of effectiveness possible

relative safety extending
even to patients on chronic
warfarin therapy¹⁹ no unacceptable
fluctuation in prothrombin time has been reported
with Dalmane



The
Dalmane[®]
(flurazepam HCl)
difference.



Please see following page for a summary of product information.


For relief of insomnia
no other sleep medication
has all the advantages of

Dalmane[®]
(flurazepam HCl) [®] 30-mg and 15-mg capsules

Objectively proved in the sleep research laboratory:

- Sleep within 17 minutes, on average
- Sleep for 7 to 8 hours, on average
- Sleep with fewer nighttime awakenings
- Continued effectiveness over 28 nights of administration

Rx Dalmane 30 mg
#30
Sig: 1 cap h s
prn



Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

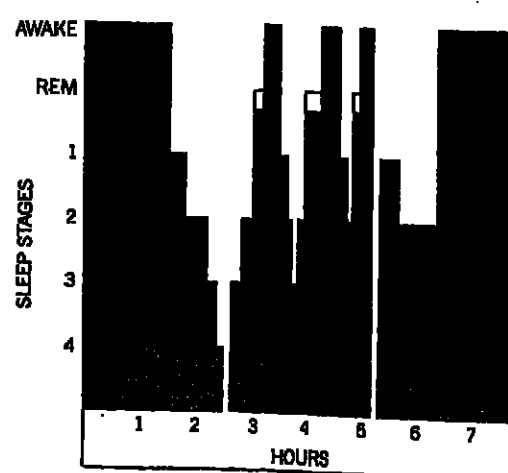
Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

REFERENCES:

1. Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
2. Kales A, et al: *Clin Pharmacol Ther* 18:356-363, Sep 1975
3. Dement WC, et al: Long-term effectiveness of flurazepam 30 mg h.s. on chronic insomniacs. Presented at the 15th annual meeting of the Association for Psychophysiological Study of Sleep, Edinburgh, Scotland, Jun 30-Jul 4, 1975
4. Frost JD Jr: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
5. Kales A, et al: Flurazepam (Dalmane), a composite of short and intermediate term studies. Presented at the 15th annual meeting of the Association for Psychophysiological Study of Sleep, Edinburgh, Scotland, Jun 30-Jul 4, 1975
6. Dement WC, Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
7. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington, DC, May 3-7, 1971
8. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
9. Robinson DS, Amidon EL: Interaction of benzodiazepines with warfarin in man, in *The Benzodiazepines*, edited by Garattini S, Mussini E, Randall LO. New York, Raven Press, 1973, p. 641



ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110



Trouble Falling Asleep,
Staying Asleep,
Sleeping Long Enough

or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Before prescribing Dalmane (flurazepam HCl), please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly

Wednesday, June 9, 1976

Clinical Trials



IMMATERIA MEDICA

Hooked on Classifieds

A Florida doctor who wants to remain nameless because he's "hooked on classifieds" has sent us the following excerpt from the classified section of the Miami Herald:

41-35 Felicitous Names

TROPICAL Pines Enterprises
16220 SW 107 Ave Mia H J Drainville
DOVAL Management 11221 SW
65 Ave Miami Jose M. Regalado.
Francisco Fernandez
SOS Electric Co 4135 W 5 Lane
Mia Fl Eugene Suslowicz
SOS Dockside Marine Services
115 NW 109 St Miami Shores Fl Vincent F. Rakus owner
KEYS Auto Appraisal P O Box 90
Big Pine Key Fl Dennis Wilson
HIGH Priest Productions P O Box
42084 Mia Fla S G Williams
(THE) New World 7852 W. 15 Ct
Hialeah, Fl Jim Voorhees

Asks our Florida friend: Who ever heard of felicitous names being advertised? But there they are, finest specimens in our tray this morning. Makes some things more mysterious than viruses.

French Style In Arkansas

Just because you haven't heard of "The Arkansas Traveler" or Chic Sale in recent years, don't give up. We pass along an item from page 5, No. 687, of the Food Drug Cosmetic Law Reports:

French bread... The Arkansas Office of the Attorney General has supported a determination made by the Arkansas Board of Health that the word "French" has no significance to bread other than the style of the loaf, and that unless the word "style" is printed in connection with the word "French" the Arkansas Drugs, Devices and Cosmetics Act is violated. The Board of Health has the power to make such a determination, and though another "trifur of fact" might have reached a contrary conclusion it cannot be said that the Board exceeded its authority in making the determination (Opinion of the Attorney General of the State of Arkansas, 112,619.35).

And here we thought that there was nothing down there but moonshiners and the original of *The Maid of the Ozarks*, that play about a bpxomy, innocent country girl that played for generations in Chicago. And now they've got "French style" bread.

WHEN CONSTIPATION IS CHRONIC

help change the pattern by facilitating regular elimination

Stimulate gentle peristalsis
With SENOKOT laxatives, regular comfortable evacuation was reported²⁻¹¹ in 93% of 629 cases of chronic constipation, including cases resistant to other therapy.

Dosage may be reduced gradually
Taken at bedtime, SENOKOT Tablets/Granules usually induce comfortable evacuation the next morning, gently and predictably. As regular elimination is established, dosage may be reduced gradually and eventually discontinued. SENOKOT Tablets/Granules are virtually colon-specific¹ and generally free of side effects at proper dosage levels.

References: 1. Godding, E. W.: *Therapeutic Agents in Management of Constipation*, edited by Sir Francis Avery Jones and Edmund W. Godding, Oxford, Blackwell Scientific Publications, 1972, p. 85. 2. Lowy, A.: *Int Rec Med* 173:303 (May) 1980. 3. Treusch, H., Rosenfeld, S.: *Am J Gastroenterol* 31:702 (June) 1969. 4. Peyton, T. R.: *J Natl Med Assoc* 49:388 (Nov.) 1957. 5. Linnphur, T. A., Ehrlich, R.: *Am J Gastroenterol* 27:281 (April) 1967. 6. Filmer, P., Woodson, G. D.: *Lancet* 1:467 (March 7) 1953. 7. Bailey, H., Camallo, R.: *Providence Med* 38:3 (Dec.) 1970. 8. Howard, L. R. C.: *Acta Gastroenterol Belg* 29:810, 1986. 9. Wanic, Choux, J.: *Sud Med & Chirurg* No. 2488 (Nov. 30) 1984. 10. Baujal, J. P.: *Gaz Hopitaux* 138e:455 (April) 1984. 11. Rounseau, G., et al: *J Quasi-Med* 18:129 (Feb. 10) 1983.

Purdue Frederick

SENOKOT tablets granules
a natural vegetable laxative

Senokot laxative claims are documented



John Morison Administration Manager
Vicki Morison Conference Manager
Isabel Hutchings Conference Assistant
Charlotte Benton-Hughes Conference Assistant
Kerry Brown Technical Services Manager

Surrey TW9 2LS
Tel: 081 332 2422
Fax: 081 332 0939